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Supplementary information

Engineered LwaCas13a with enhanced collateral activity for nucleic acid detection

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Supplementary Information

Engineered LwaCas13a with Enhanced Collateral Activity for Nucleic Acid Detection

Jie Yang[1,10], Yang Song[2,3,10], Xiangyu Deng[4], Jeffrey A. Vanegas[1], Zheng You[1], Yuxuan Zhang[2,3], Zhengyan Weng[2,3], Lori Avery[5], Kevin D. Dieckhaus[6], Advaith Peddi[4], Yang Gao[4]*, Yi Zhang[2,7]*, Xue Gao[1,8,9]*

1 Department of Chemical and Biomolecular Engineering, Rice University, Houston, TX, USA.

2 Department of Biomedical Engineering, University of Connecticut, Storrs, CT, USA

3 Institute of Materials Science, University of Connecticut, Storrs, CT, USA

4 Department of Bioscience, Rice University, Houston, TX, USA.

5 Department of Pathology and Laboratory Medicine, UConn Health, Farmington, CT, USA

6 Division of Infectious Diseases, Department of Medicine, UConn Health, Farmington, CT, USA

7 Polymer Program, Institute of Materials Science, University of Connecticut, Storrs, CT, USA

8 Department of Bioengineering, Rice University, Houston, TX, USA.

9 Department of Chemistry, Rice University, Houston, TX, USA.

10 These authors contributed equally.

* Corresponding Author: xue.gao@rice.edu (X.G.), yi.5.zhang@uconn.edu (Y.Z.), yg60@rice.edu (Y.G.).

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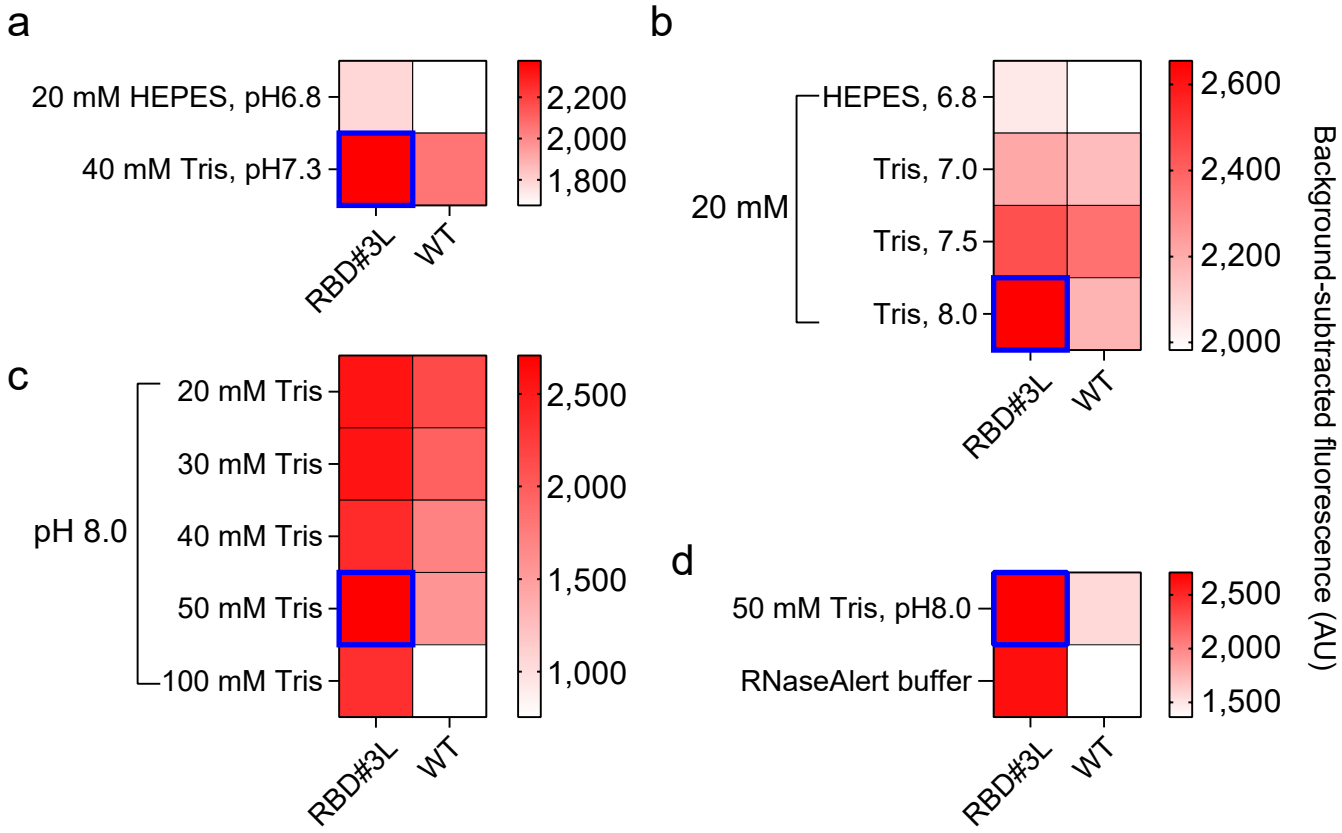
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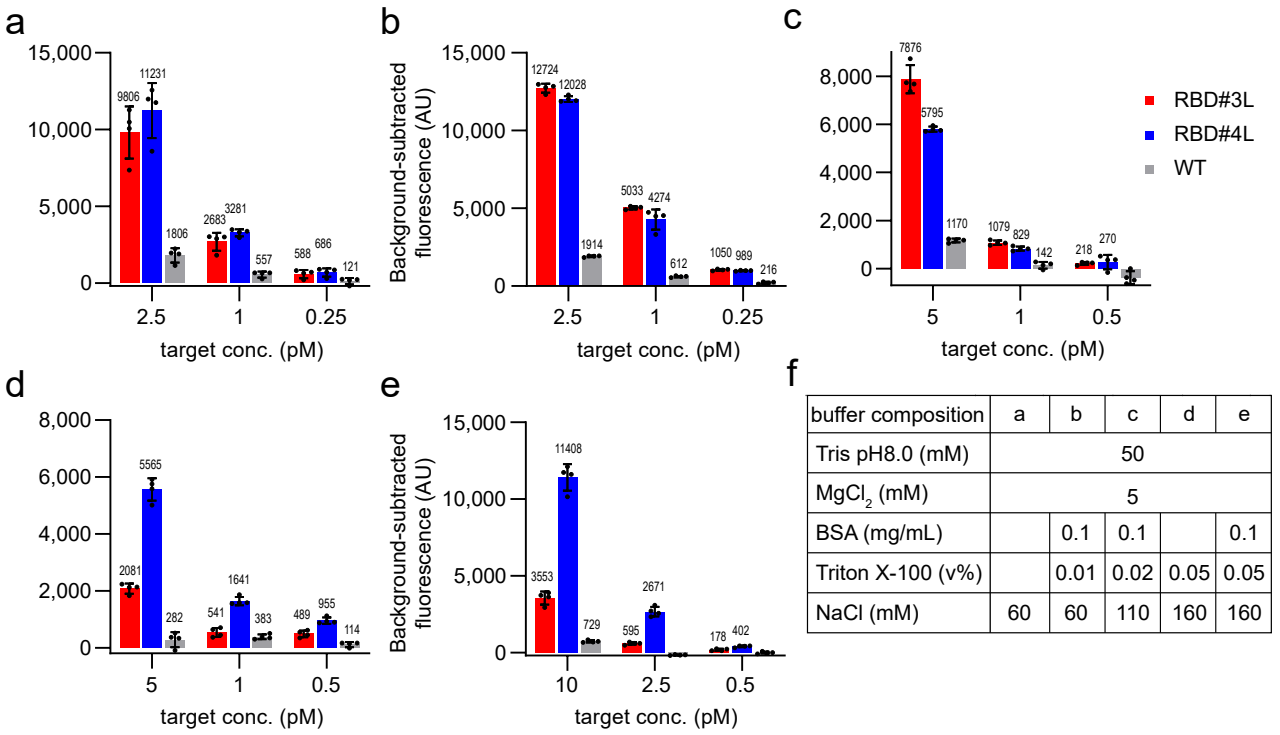
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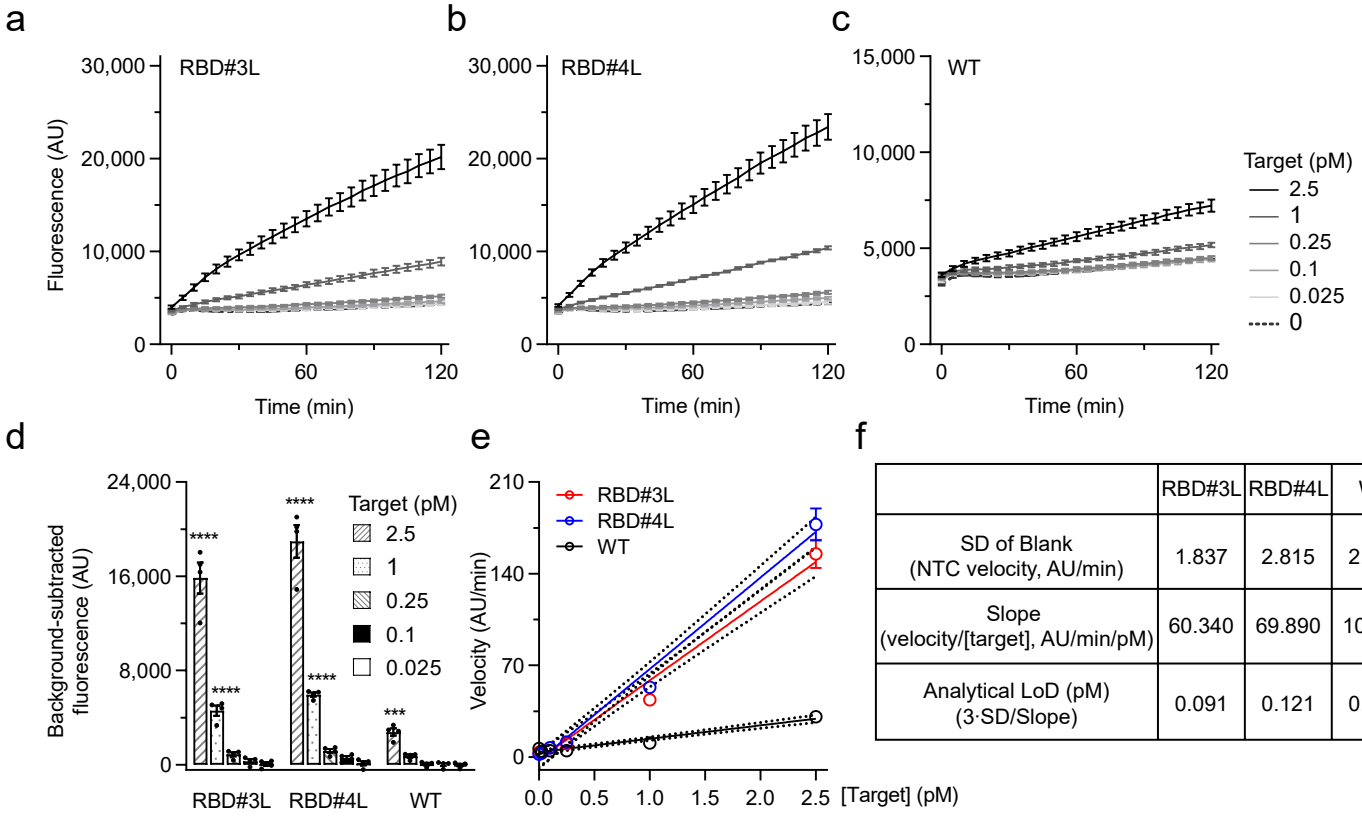


Supplementary Figure 1. Optimization of reaction buffer.
Background-subtracted fluorescence using various reaction buffers after a 2-h reaction. The RNPs were formed as described in Methods, the reporter (U_{11}) was 125 nM. The Mg^{2+} was 5 mM. The target is a 10 pM SARS-CoV-2 N gene fragment (T1). Various concentrations and pHs of Tris and HEPES buffers were tested. **a**, Comparison between two previously used buffering conditions, 20 mM HEPES, pH 6.8, and 40 mM Tris, pH7.3. **b**, Comparison of various pH values, 6.8, 7.0, 7.5 and 8.0. The buffer concentrations were all 20 mM. **c**, Comparison of various concentrations of Tris buffer (pH 8.0), 20, 30, 40, 50 and 100 mM. **d**, Comparison between 50 mM Tris pH 8.0 buffer and commercial RNaseAlert buffer. For **a–d**, means were calculated from three or four technical replicates. The highest values are labeled with blue squares.



buffer composition	a	b	c	d	e
Tris pH8.0 (mM)	50				
$MgCl_2$ (mM)	5				
BSA (mg/mL)		0.1	0.1		0.1
Triton X-100 (v%)		0.01	0.02	0.05	0.05
NaCl (mM)	60	60	110	160	160

Supplementary Figure 2. BSA, Triton X-100, and salt concentration affect collateral activity. Background-subtracted fluorescence in the detection of SARS-CoV-2 N gene synthetic target (T1). **a–e,** Bar graphs are the 60-min background-subtracted fluorescence mean ± s.e.m. from four technical replicates. The mean values were labeled on the top of each bar. Target concentrations are as indicated. **f,** Reaction buffer compositions of **a–e**.

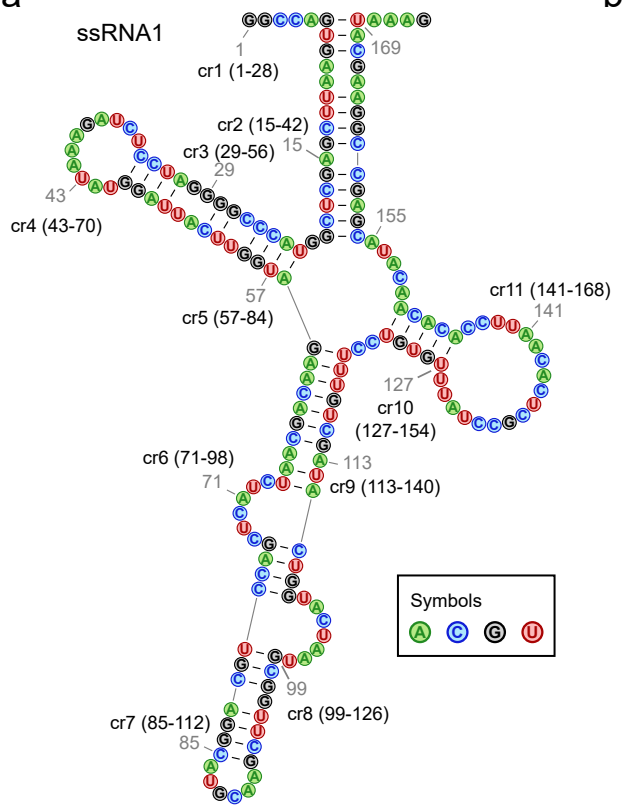


	RBD#3L	RBD#4L	WT
SD of Blank (NTC velocity, AU/min)	1.837	2.815	2.713
Slope (velocity/[target], AU/min/pM)	60.340	69.890	10.210
Analytical LoD (pM) (3·SD/Slope)	0.091	0.121	0.797

Supplementary Figure 3. LoD analysis of RBD#3L, RBD#4L and WT LwaCas13a in Tris buffer.

a–c, Raw fluorescence data measured for 120 min, expressed as mean ± s.e.m. from four technical replicates. RBD#3L, RBD#4L, and WT LwaCas13a were complexed with crRNA (cr1) in reaction buffer as in **Fig. S2a** and tested with 2.5, 1, 0.25, 0.1, 0.025 pM of the synthetic RNA (T1). The 0 pM target samples were used as no-target control (NTC). **d**, Bar plot represented the 120-min background-subtracted fluorescence expressed as mean ± s.e.m. from four technical replicates. Adjusted *p* values were calculated using two-way ANOVA with Dunnett's test: ns, not significant, $^{***}p$=0.0008, $^{****}p$<0.0001, compared to background signal (NTC) (see SourceData for adjusted *p* value). **e,** The velocities of each reaction within 60 min were obtained by linear regression from **a–c** and were expressed as mean ± s.e.m. from four technical replicates and plotted as a function of the target concentration. **f,** Analytical LoD of three proteins was calculated using the equation: $LoD = 3 \cdot SD_{NTC} / Slope$. SD_{NTC} was the standard derivation of the reaction velocity from the no-target control samples. The slope was determined by linear regression of the reaction velocity against target concentration from **e**.

a

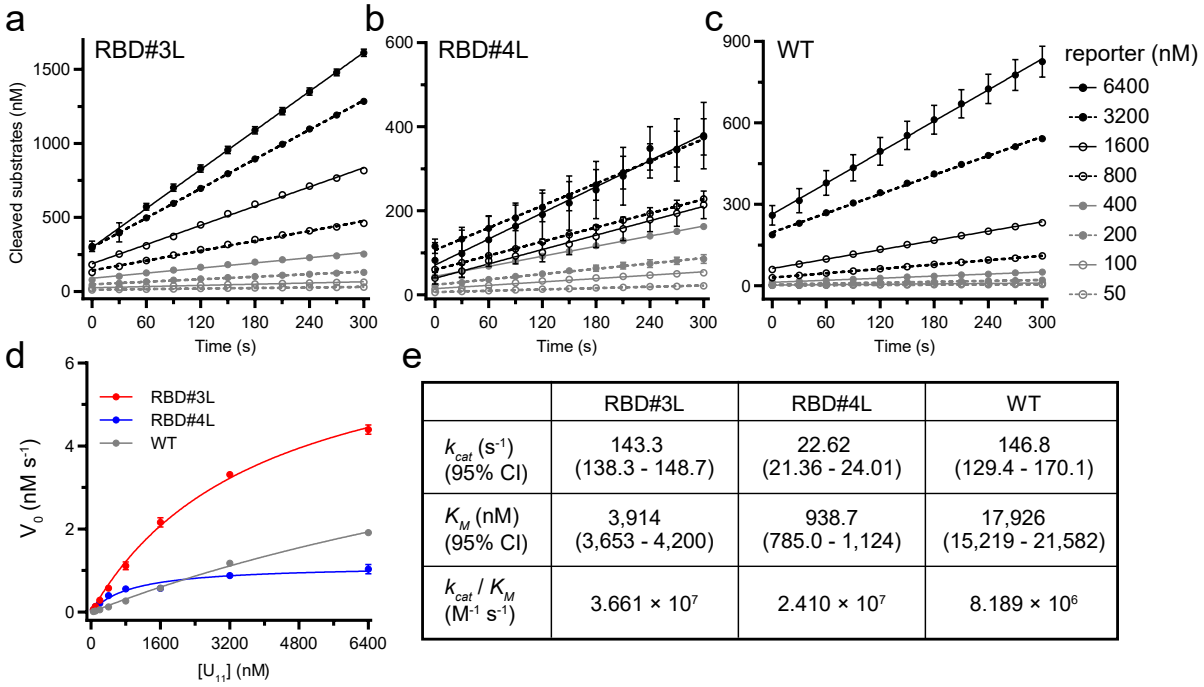


b

```
PM      5’-CGCAUUACGUUUGGUGGACCCUCAGAUU-3’
            1                           28
MM2         CCCAUUACGUUUGGUGGACCCUCAGAUU
MM4         CGCUUUACGUUUGGUGGACCCUCAGAUU
MM6         CGCAUAACGUUUGGUGGACCCUCAGAUU
MM8         CGCAUUAGGUUUGGUGGACCCUCAGAUU
MM10        CGCAUUACGCUUGGUGGACCCUCAGAUU
MM12        CGCAUUACGUUAGGUGGACCCUCAGAUU
MM14        CGCAUUACGUUUGCUGGACCCUCAGAUU
MM16        CGCAUUACGUUUGGUCGACCCUCAGAUU
MM18        CGCAUUACGUUUGGUGGUCCCUCAGAUU
MM20        CGCAUUACGUUUGGUGGACGCUCAGAUU
MM22        CGCAUUACGUUUGGUGGACCCACAGAUU
MM24        CGCAUUACGUUUGGUGGACCCUCUGAUU
MM26        CGCAUUACGUUUGGUGGACCCUCAGUUU
MM28        CGCAUUACGUUUGGUGGACCCUCAGAUA

DM1         GCCATTACGTTTGGTGGACCCTCAGATT
DM5         CGCAAAACGTTTGGTGGACCCTCAGATT
DM9         CGCATTACCATTGGTGGACCCTCAGATT
DM13        CGCATTACGTTTCCTGGACCCTCAGATT
DM17        CGCATTACGTTTGGTGCTCCCTCAGATT
DM21        CGCATTACGTTTGGTGGACCGACAGATT
DM25        CGCATTACGTTTGGTGGACCCTCACTTT
            1                           28
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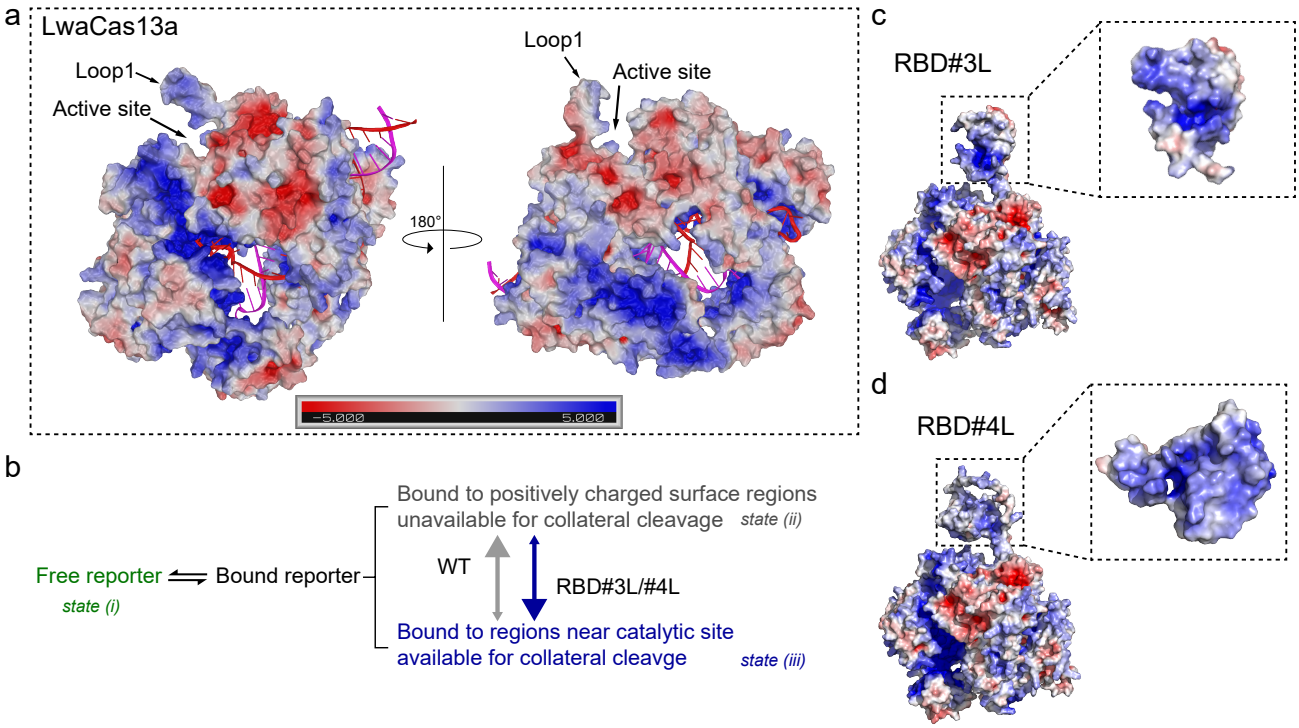
Supplementary Figure 4. Sequences related to programmability and specificity tests. **a**, ssRNA1 target (T3) and 11 crRNAs (cr4–14) tiling along the sequence. **b,** Single-point mutations at every two nucleotides (MM2–MM28, T5–T18) and double-point mutations (DM1–DM25, T19–T25) at every four nucleotides were introduced to the 28-nt synthetic SARS-CoV-2 N gene fragment target (PM, T4).



	RBD#3L	RBD#4L	WT
k_{cat} (s^{-1}) (95% CI)	143.3 (138.3 - 148.7)	22.62 (21.36 - 24.01)	146.8 (129.4 - 170.1)
K_M (nM) (95% CI)	3,914 (3,653 - 4,200)	938.7 (785.0 - 1,124)	17,926 (15,219 - 21,582)
k_{cat} / K_M (M^{-1} s^{-1})	3.661×10^7	2.410×10^7	8.189×10^6

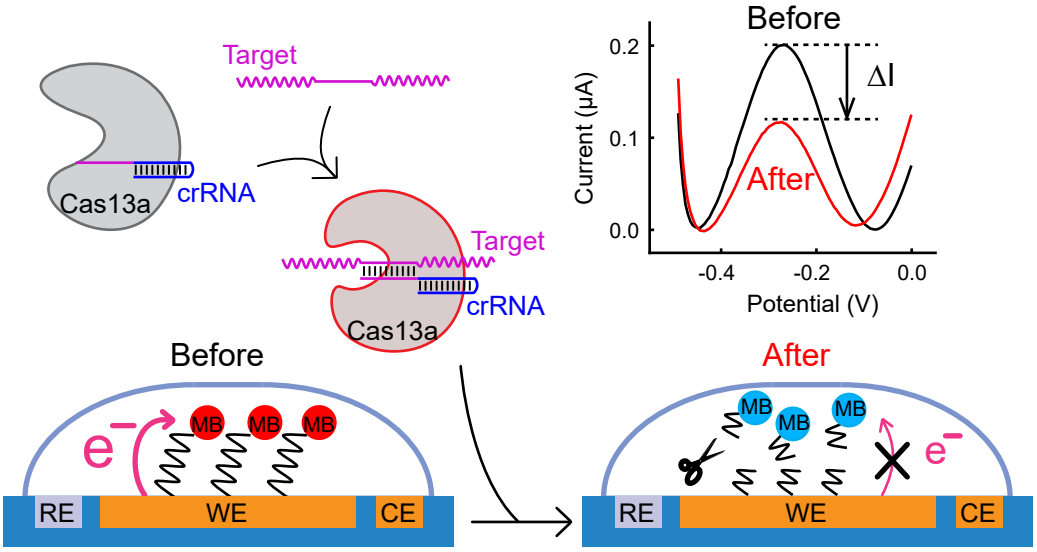
Supplementary Figure 5. Kinetic analysis of RBD#3L, RBD#4L, and WT LwaCas13a in reactions supplemented with BSA and Triton X-100.

a–c, Progress curves of cleaved reporters versus time. Data were plotted as mean ± s.e.m. from four technical replicates. The RNP complex of RBD#3L, RBD#4L, and WT in reaction buffer as in **Fig. S2b** were incubated with 50 pM of the targets (T1) for 10 min at 37°C prior to cleavage reaction using 6400, 3200, 1600, 800, 400, 200, 100 and 50 nM of the U_{11} substrates. The initial velocities (within 300 s) of each reaction were obtained by linear regression. **d,** Initial velocities obtained from **a–c** were plotted as mean ± s.e.m. from four technical replicates versus the U_{11} reporter concentration and fit to a Michaelis-Menten curve. **e,** Summary of kinetic parameters obtained from **d**. Values of k_{cat} and K_M were expressed as mean with 95% CI.

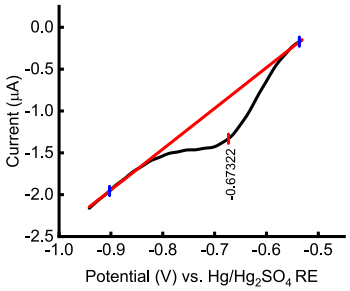


Supplementary Figure 6. Electrostatic surface potential and proposed reporter binding patterns.

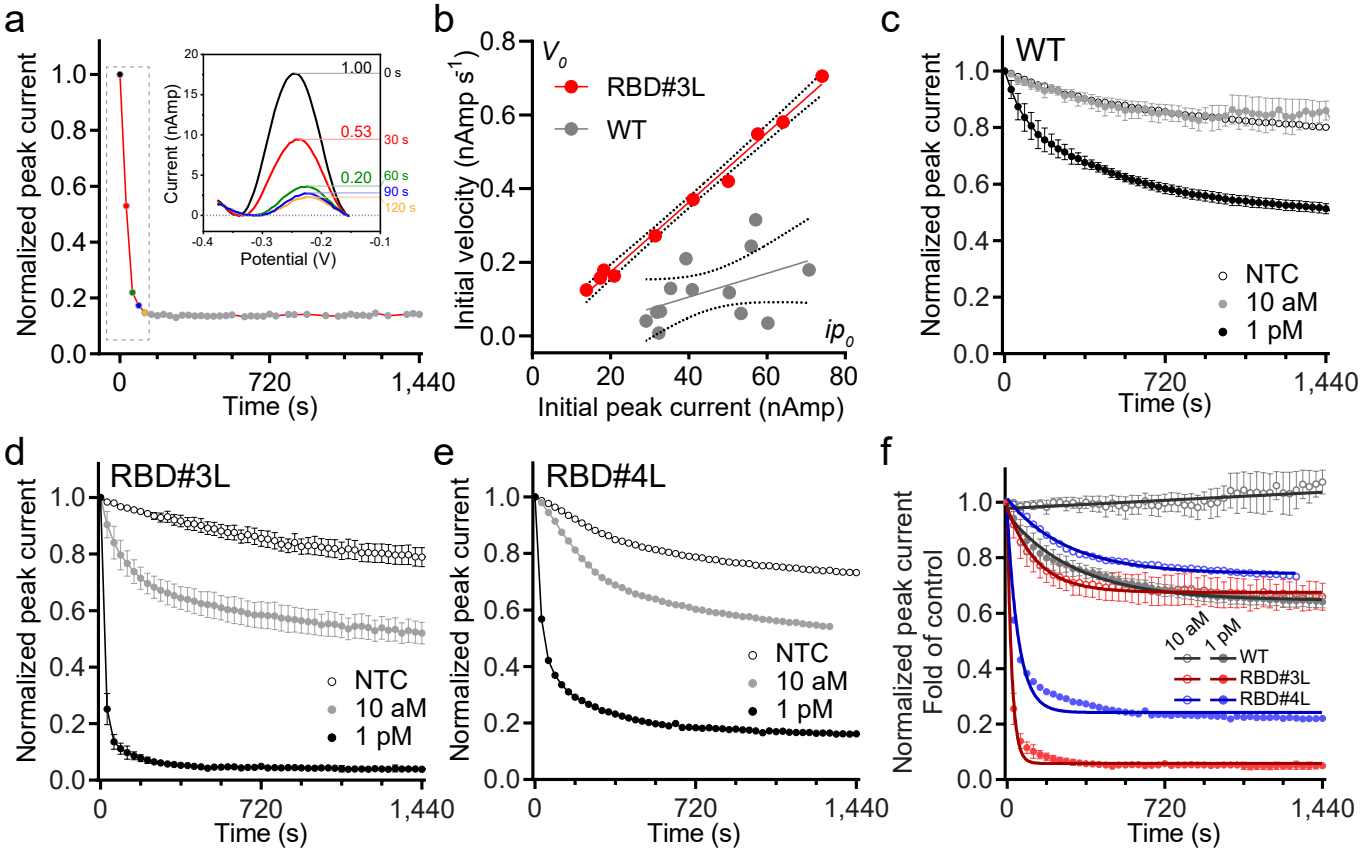
a, Surface views of the predicted LwaCas13a from **Fig. 2b**. There are positive charges near the central channel for crRNA and target RNA binding as well as on other regions of the protein surface, which may interact with any surrounding RNAs in a sequence-independent manner. Non-specific RNAs may stabilize the apo-form protein through neutralizing effects and electrostatic interactions[1]. **b,** Reporters in fluorescence Cas13a assay are either at a free state (i) in the solution, or bound with protein. The bound reporters may either bind to active site distal regions unavailable for cleavage (ii), or active site proximal regions ready for cleavage (iii). Inserting an RBD to the active site-proximal Loop 1 would probably increase the proportion of state (iii) RNA reporter and therefore improve the collateral cleavage efficiency. Additional strategies to reduce state (ii) reporters, which may bind to the protein surface without being cleaved due to the distance from active sites, would also increase the collateral cleavage efficiency. **c and d,** Surface views of the AlphaFold[2] predicted RBD#3L (**c**) and RBD#4L (**d**). Insets: surface views of RBD#3 (PDB: 5MPL) and RBD#4 (PDB: 2MXY) from **Fig. 2e, f**.



Supplementary Figure 7. Schematic of CRISPR-Cas13 based electrochemical sensor. The screen-printed electrode (SPE) is comprised of three electrodes, which are gold (Au) as the working electrode (WE) and counter electrode (CE), and Ag as a pseudo-reference electrode (RE). The WE is functionalized by tethering thiol-linked U_{20} with 3'-methylene blue (MB). The electron transfer between WE and the MB is acquired by square wave voltammetry (SWV). The applied negative potential on the electrode and the negatively charged reporter RNA backbone with close-packed passivator 6-mercapto-1-hexanol (MCH) molecule can lead to the formation of a monolayer of fully extended PolyU lining up on the surface[3]. This results in a distinct RNA conformation relative to the free RNA reporter in solution, providing a compact interface for protein complex and reporter interaction, which would be restricted to a minimal level and occur only at the protein–reporter interface, effectively reducing the proportion of state (ii) reporter (**Supplementary Figure 6b**). The affinity between fused RBD and the reporters may facilitate protein binding with the immobilized reporters, leading to efficient collateral cleavage of the reporters. In contrast, due to the constrained protein–RNA binding and lack of an RBD, the WT may interact less and in a disorganized manner with the immobilized reporters. Before adding the target, the protein:crRNA complex is not activated, and the tethered reporters will remain intact, resulting in a high electrochemical current of MB. After adding the target, the transduced signal decreases due to the loss of MB by collateral cleavage of the U_{20} linker. The difference of current (ΔI) before and after adding the target reflects the collateral activity, showing a target concentration-dependent manner of signal change.

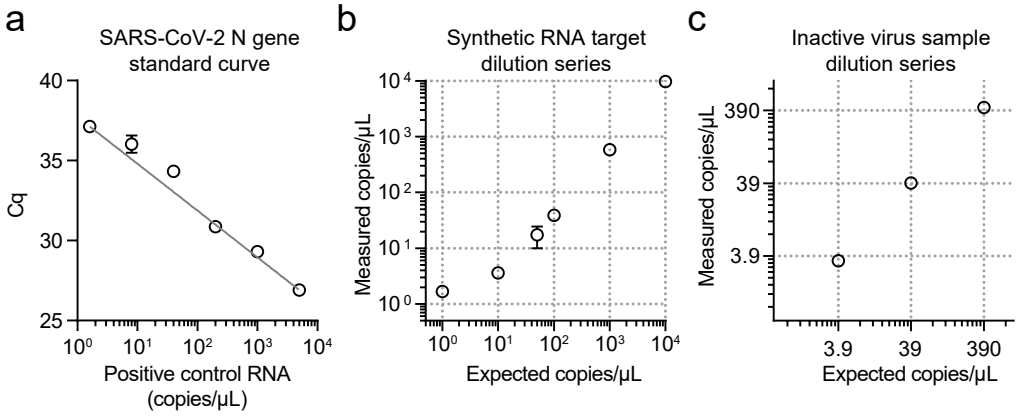


Supplementary Figure 8. Measurement of surface reporter density.
The reporter probe density was calculated by using the cyclic voltammetry measurement. Reporter functionalized SPE was scanned between -0.95–0.45 V versus the Hg/Hg_2SO_4 RE at a 50 mV/s scan rate. The reduction peak area of methylene blue (4.93×10^{-7} AV) was integrated using OriginLab software. After being divided by the scan rate (50 mV/s), the charge (Q) was 9.87×10^{-6} C (Q = peak area / scan rate = (4.93×10^{-7} AV) / (50 mV/s) = 9.87×10^{-6} C). The equation to calculate the reporter probe amount was $\Gamma = Q / (n \cdot A \cdot F)$; where n is equal to 2, A is the working electrode surface area (2.0 mm^2), and F is the Faraday's constant (96485 C/mol). The reporter density (Γ) was estimated to be 25 $pmol/mm^2$. The total amount of functionalized reporter on the WE was estimated to be 50 pmol.

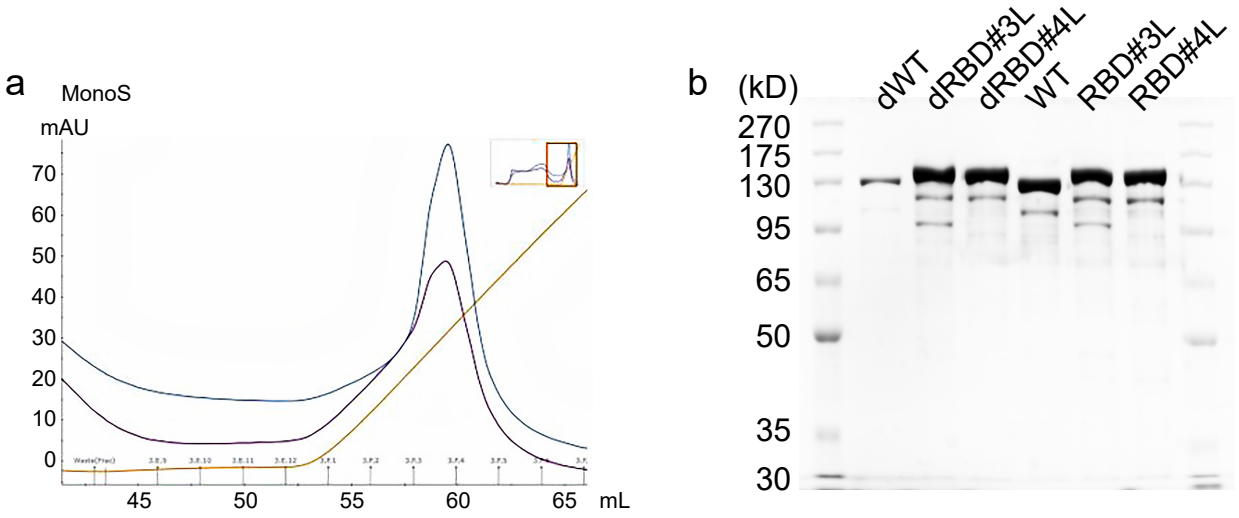


Supplementary Figure 9. Investigation of electrochemical kinetics.
a, Representative images of peak current acquired by SWV scans. The initial peak current (ip_0) was measured with electrolyte buffer containing 10 mM Tris-HCl (pH 8.0) and 100 mM NaCl before adding the CRISPR reaction onto the sensor. The CRISPR reactions were assembled as described in Method and gently dispersed in the electrolyte. Inset is the overlapped responsive peak current measured by consecutive SWV scans with 30 s intervals (ip_t, t = 30, 60, 90……). **b,** Analysis of initial velocity (V_0, nAmp/s) as a function of the initial peak current (ip_0, nAmp). The time course voltammetric responses were recorded every 30 s within 2 min to get a linear relationship between the peak current and the time duration. V_0 was calculated as the change of peak current per second (nAmp/s). The target concentration was 1 pM for both reactions using RBD#3L and the WT. Dots are experimentally measured values. Solid lines are the fitted simple linear regression. Dashed lines represent 95% CI (GraphPad). A linear relationship between V_0 and ip_0 in reactions using RBD#3L implied a first-order kinetics and a constrained reporter–protein interaction. Meanwhile, no obvious curve fitting pattern can be seen between V_0 and ip_0 in reactions using the WT. The difference in V_0–ip_0 relationship between the RBD#3L and the WT revealed that the interactions between the fused RBD and the immobilized reporters could be the major driving force for collateral cleavage of the reporters on the sensor. The severely restricted protein–reporter interactions might lead to unfavorable kinetics and large signal fluctuations in WT-mediated reactions. **c–e,** Time-course curves of electrochemical measurement of 1 pM and 10 aM targets and no-target control (NTC) using the WT (**c**), RBD#3L (**d**), and RBD#4L (**e**). The peak current at each time point was normalized to the corresponding ip_0. The connected circles with error bars in **c–e** are mean ± s.e.m from three or four replicates or mean from two replicates (n = 2–4). **f,** Fold change of the normalized on-target peak current to the corresponding normalized

no-target control (NTC) peak current at each time point (Fold = $(ip_t / ip_0)_{target} / (ip_t / ip_0)_{NTC}$). The normalized peak current was mean ± s.e.m. of four replicates for WT and RBD#3L, and mean of two replicates for RBD#4L from **c–e**. Lines are one-phase decay curve fitting (GraphPad). The SARS-CoV-2 N gene fragment synthetic RNA target was used in **a–f**.



Supplementary Figure 10. RT-qPCR quantification of target RNA.
a, Measured Cq values of standard positive controls (IDT) with concentrations of 5000, 1000, 200, 40, 8 and 1.6 copies/µL. **b,** synthetic RNA targets, and **c,** inactive viruses were serially diluted, measured by RT-qPCR, and interpolated from the standard curve from **a**. The expected concentration was calculated from stock concentration either determined by using Nanadrop (**a**), or provided by the vendor's ddPCR analysis (**b**). **a–c,** Points and errors represented mean ± s.d. from three technical replicates.



Supplementary Figure 11. Protein purification of active and inactive RBD#3L, RBD#4L, and WT LwaCas13a.

a, Cation exchange chromatography of LwaCas13a proteins. **b,** SDS-PAGE image of purified proteins from a single run.

Supplementary Table 1

List of candidate RBDs. The PDB ID, Uniprot accession number (with amino acid residue positions in the original protein), and length of the domain are listed.

No.	RNA binding domains (RBDs)	PDB	Uniprot	Length (aa)
1	DRBM3_ADAR1	2MDR	P55265 (708 – 801)	94
2	RRM1_HNRNPA1	5MPG	P09651 (1 – 104)	104
3	RRM2_HNRNPA1	5MPL	P09651 (98 – 196)	99
4	RRM_HNRNPC	2MXY	P07910 (2 – 106)	105
5	ZnF1/2_METTL3	5YZ9	Q86U44 (259 – 357)	99
6	Zα_ADAR1	3F21	P55265 (126 – 202)	77
7	Zβ_ADAR1	1XMK	P55265 (293 – 366)	74

Supplementary Table 2

LoD of RBD#3L, RBD#4L, and WT LwaCas13a in reactions supplemented with BSA and Triton X-100. Analytical LoD of three proteins was calculated using the equation: LoD = $3 \cdot SD_{NTC}$ / Slope. SD_{NTC} was the standard deviation of the reaction velocity from the no-target control samples. The slope was determined by linear regression of the reaction velocity against target concentration from **Extended Data Fig. 4e**.

	RBD#3L	RBD#4L	WT
SD_{NTC} of velocity (AU/min)	0.236	0.342	0.918
Slope (velocity/[target], AU/min/pM)	80.980	77.700	9.733
Analytical LoD ($3 \cdot SD_{NTC}$/slope, pM)	0.009	0.013	0.283

Supplementary Table 3

Dissociation constant (K_D) for target and reporter RNA binding with RBD#3L, RBD#4L and the WT. Means with 95% CI calculated from **Extended Data Fig. 5** are listed.

Protein (dHEPN2)	$K_{D,\ target\text{-}36}$ (nM) (95% CI)	$K_{D,\ target\text{-}105}$ (nM) (95% CI)	$K_{D,\ reporter}$ (μM) (95% CI)
RBD#3L	23.62 (20.21 – 28.86)	11.42 (10.11 – 13.16)	0.2339 (0.2162 – 0.2545)
RBD#4L	18.85 (16.76 – 21.57)	12.81 (11.60 – 14.28)	0.1526 (0.1424 – 0.1634)
WT	46.04 (31.83 – 89.06)	15.78 (11.24 – 32.23)	0.4719 (0.4104 – 0.5569)

Supplementary Table 4

Michaelis-Menten kinetic parameters in reactions using RBD#3L, RBD#4L and the WT. Values of k_{cat} and K_M (mean with 95% CI) were calculated from **Extended Data Figure 6**.

	RBD#3L	RBD#4L	WT
k_{cat} (s^{-1}) (95% CI)	33.50 (32.72 – 34.31)	7.486 (7.341 – 7.634)	27.78 (26.39 – 29.34)
K_M (nM) (95% CI)	1,923 (1,817 – 2,037)	483.6 (450.7 – 518.9)	7,070 (6,504 – 7,711)
k_{cat}/K_M ($M^{-1}\cdot s^{-1}$)	1.742×10^7	1.548×10^7	3.929×10^7

Supplementary Table 5

Quantification of positive clinical samples (Mean ± s.d. from three replicates)

	RT-qPCR quantification[a]	Concentration in Cas13 reactions[b]	
	Cq (N = 3)	copies/µL	conc. (aM)
P1	24.674 ± 0.157	4163.369 ± 505.348	6913.437 ± 839.15
P2	22.073 ± 0.044	32065.723 ± 1103.003	53246.387 ± 1831.579
P3	26.203 ± 0.087	1244.741 ± 86.619	2066.941 ± 143.834
P4	22.33 ± 0.029	26193.541 ± 598.641	43495.398 ± 994.067
P5	30.566 ± 0.067	40.18 ± 2.075	66.721 ± 3.446
P6	28.298 ± 0.212	241.447 ± 41.901	400.932 ± 69.578
P7	25.200 ± 0.053	2737.965 ± 113.221	4546.498 ± 188.008
P8	26.011 ± 0.123	1450.974 ± 144.251	2409.399 ± 239.535
P9	32.072 ± 0.107	12.296 ± 1.061	20.417 ± 1.762
P10	25.954 ± 0.143	1518.333 ± 173.268	2521.252 ± 287.719
P11	34.477 ± 0.185	1.863 ± 0.280	3.093 ± 0.465

[a] RT-qPCR quantification was performed using purified and concentrated RNA as input.
[b] Cas13–electrochemical biosensor reactions were performed using unextracted VTM samples with a 5-min quick treatment as input.

Supplementary Table 6

Simulation sample preparation.

Targets	Biofluids	Heating steps	Final concentrations	Related figures
SARS-CoV-2 N gene (T1)	VTM	Incubated at 40°C for 5 min, combined with target RNA and bgRNA, and heated at 70°C for 5 min	10 pM targets, 8% VTM, and 50 ng bgRNA	Fig. 5a and Extended Data Fig. 7a
			50 pM targets, 16% or 8% VTM, and 50 ng bgRNA	Extended Data Fig. 8a
	Saliva	incubated at 40°C for 5 min, combined with target RNA and bgRNA, and heated at 95°C for 5 min	10 pM targets, 8% saliva, and 50 ng bgRNA ().	Fig. 5a and Extended Data Fig. 7b
Zika (T28)	Urine	incubated at 50°C for 20 min, combined with target RNA and bgRNA, and heated at 95°C for 5 min	10 pM targets, 8% urine, and 50 ng bgRNA	Fig. 5b and Extended Data Fig. 7c
			50 pM targets, 16% or 8% urine, and 50 ng bgRNA	Extended Data Fig. 8b
Dengue (T29)	Serum	incubated at 42°C for 20 min, combined with target RNA and bgRNA, heated at 64°C for 5 min, and spun down shortly to remove any aggregates.	10 pM targets, 2.5% serum, and 50 ng bgRNA	Fig. 5c and Extended Data Fig. 7d
			50 pM targets, 4.8% or 2.5% serum, and 50 ng bgRNA	Extended Data Fig. 8c
Ebola (T30)	Plasma	incubated at 37°C for 20 min, combined with target RNA and bgRNA, heated at 95°C for 10 min, and spun down shortly to remove any aggregates.	10 pM targets, 2.5% plasma, and 50 ng bgRNA	Fig. 5d and Extended Data Fig. 7e.
			50 pM targets, 4.8% or 2.5% plasma, and 50 ng bgRNA	Extended Data Fig. 8d
miR-19b (T31)	Serum or Plasma	incubated at 50°C for 20 min and 65°C for 5 min, and combined with target RNA and bgRNA	10 pM targets, 2.5% serum or plasma, and 50 ng bgRNA	Fig. 5e and Extended Data Fig. 7f, g
miR-2392 (T32)	Serum	incubated at 50°C for 20 min and 65°C for 5 min, the urine samples were	200 pM targets, 2.5% serum, and 50 ng bgRNA	Fig. 5f and Extended Data Fig. 7h
	[a]Urine	incubated at 50°C for 20 min and heated at 95°C for 5 min.	200 pM targets, 8% urine, and 50 ng bgRNA	Fig. 5f and Extended Data Fig. 7i

Supplementary Table 7

Preparation of CRISPR-Cas13a master mix in HEPES and Tris buffers for Cas13–electrochemical measurement.

No. of steps	CRISPR reaction in HEPES buffer	CRISPR reaction in Tris buffer
(1)	Nuclease- free water	Nuclease- free water
(2)	20 mM HEPES, pH6.8	50 mM Tris-HCl, pH 8.0
(3)	9 mM $MgCl_2$	5 mM $MgCl_2$
(4)	45 nM protein	45 nM protein
(5)	2 U/μL RNase Inhibitor	1 U/μL RNase Inhibitor
(6)	22.5 nM crRNA	22.5 nM crRNA
(7)	Incubated for 10 min in the dark at room temperature	
(8)	various concentrations of target	various concentrations of target
Final Volume	20 μL	20 μL

Supplementary Notes

1. Amino acid sequences of wild-type LwaCas13a and RBD-LwaCas13a fusions

Color coding is as follows:
RBDs; linkers; LwaCas13a (WT); **Loop1 insertion sites**; **Loop 2 insertion site**

(1) LwaCas13a (WT)
MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVK**NNKG**EEK
YVSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFN
LELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKN
TKFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLN
KFVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQD
KEEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILK
NYEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQ
SANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKI
YFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQ
NLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRL
VGYTSIWERDLRFRLKGEFPENHYIEEIFNFDN**SK**NVKYKSGQIVEKYINFYKELYKDNV
EKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAI
MKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVK
VMFEYKALE

Loop 1 N415/N416 fusions
(2) RBD#1L
MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVK**N**MMPNKV
RKIGELVRYLNTNPVGGLLEYARSHGFAAEFKLVDQSGPPHEPKFVYQAKVGGRWFPA
VCAHSKKQGKQEAADAALRVLIGENEKAER**NKG**EEKYVSGEVDKIYNENKQNEVKEN
LKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNLELEGKDIFAFKNIAPSEISKKM
FQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNTKFNFVNKNIPFVPSFTKLYNKI
EDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNKFVKNSKVFFKITNEVIKINKQR
NQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDKEEKNTYIDFIQQIFLKGFIDYLN
KNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKNYEKHNRNKEIPHEINEFVREIKL
GKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQSANKEETFSDELELINLLNLDNNR

VTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKIYFDGENIIKHRAFYNIKKYGMLN
LLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQNLHRKYARPKKDEKFNDEDYKE
YEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRLVGYTSIWERDLRFRLKGEFPENH
YIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVKKLKQEKKDLYI
RNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYGFVATFKIGADK
KIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

(3) RBD#2L
MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNMSKSESP
KEPEQLRKLFIGGLSFETTDESLRSHFEQWGTLTDCVVMRDPNTKRSRGFGFVTYATVE
EVDAAMNARPHKVDGRVVEPKRAVSREDSQRPGAHLTVNKGEEKYVSGEVDKIYNEN
KQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNLELEGKDIFAFKNI
APSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNTKFNFVNKNIPFVP
SFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNKFVKNSKVFFKITN
EVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDKEEKNTYIDFIQQIF
LKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKNYEKHNRNKEIPHE
INEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQSANKEETFSDELELI
NLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKIYFDGENIIKHRAFY
NIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQNLHRKYARPKKDE
KFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRLVGYTSIWERDLRF
RLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVKK
LKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYGF
VATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

(4) RBD#3L
MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNPGAHLTV
KKIFVGGIKEDTEEHHLRDYFEQYGKIEVIEIMTDRGSGKKRGFAFVTFDDHDSVDKIVI
QKYHTVNGHNCEVRKALSKQEMASASSSQRGRNKGEEKYVSGEVDKIYNENKQNEVK
ENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNLELEGKDIFAFKNIAPSEISK
KMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNTKFNFVNKNIPFVPSFTKLY
NKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNKFVKNSKVFFKITNEVIKIN
KQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDKEEKNTYIDFIQQIFLKGFID
YLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKNYEKHNRNKEIPHEINEFVR
EIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQSANKEETFSDELELINLLNLD

NNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKIYFDGENIIKHRAFYNIKKYG
MLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQNLHRKYARPKKDEKFNDED
YKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRLVGYTSIWERDLRFRLKGEFP
ENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVKKLKQEKK
DLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYGFVATFKIG
ADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

(5) RBD#4L
MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNASNVTNK
TDPRSMNSRVFIGNLNTLVVKKSDVEAIFSKYGKIVGCSVHKGFAFVQYVNERNARAA
VAGEDGRMIAGQVLDINLAAEPKVNRGKAGVKRSAAEMYGNKGEEKYVSGEVDKIYN
ENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNLELEGKDIFAF
KNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNTKFNFVNKNIP
FVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNKFVKNSKVFFK
ITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDKEEKNTYIDFIQ
QIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKNYEKHNRNKEIP
HEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQSANKEETFSDELE
LINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKIYFDGENIIKHRAF
YNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQNLHRKYARPKKD
EKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRLVGYTSIWERDLR
FRLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVK
KLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYG
FVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

(6) RBD#5L
MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNSIVEKFRS
RGRAQVQEFCDYGTKEECMKASDADRPCRKLHFRRIINKHTDESLGDCSFLNTCFHMD
TCKYVHYEIDACMDSEAPGSKDHTPSQELALTQNKGEEKYVSGEVDKIYNENKQNEVK
ENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNLELEGKDIFAFKNIAPSEISK
KMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNTKFNFVNKNIPFVPSFTKLY
NKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNKFVKNSKVFFKITNEVIKIN
KQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDKEEKNTYIDFIQQIFLKGFID
YLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKNYEKHNRNKEIPHEINEFVR
EIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQSANKEETFSDELELINLLNLD

NNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKIYFDGENIIKHRAFYNIKKYG
MLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQNLHRKYARPKKDEKFNDED
YKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRLVGYTSIWERDLRFRLKGEFP
ENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVKKLKQEKK
DLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYGFVATFKIG
ADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

(7) RBD#6L
MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNLSSHFQE
LSIYQDQEQRILKFLEELGEGKATTAHDLSGKLGTPKKEINRVLYSLAKKGKLQKEAGTP
PLWKIAVSTQNKGEEKYVSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFF
ANIDEAISSIRHGIVHFNLELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSA
NVFNYYEKDVIIKYLKNTKFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEK
DAQIYLLKNIYYGEFLNKFVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVP
VEYLAIIQSREMINNQDKEEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFS
KIKIKKDNKEKYDKILKNYEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLL
NHKELTNLKGSLEKYQSANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNE
NKIKDRKELKKFDTNKIYFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKE
YSNKKNEIEKNYTMQQNLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEF
NELNLLQGLLLKILHRLVGYTSIWERDLRFRLKGEFPENHYIEEIFNFDNSKNVKYKSGQI
VEKYINFYKELYKDNVEKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVL
ENLRKLLSYDRKLKNAIMKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKK
KLMTDRNSEELCELVKVMFEYKALE

(8) RBD#7L
MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNFLDMAEI
KEKICDYLFNVSDSSALNLAKNIGLTKARDINAVLIDMERQGDVYRQGTTPPIWHLTDK
KRERMQIKNKGEEKYVSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFA
NIDEAISSIRHGIVHFNLELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSAN
VFNYYEKDVIIKYLKNTKFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKD
AQIYLLKNIYYGEFLNKFVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPV
EYLAIIQSREMINNQDKEEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKI
KIKKDNKEKYDKILKNYEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLN
HKELTNLKGSLEKYQSANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNEN

KIKDRKELKKFDTNKIYFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEY
SNKKNEIEKNYTMQQNLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFN
ELNLLQGLLLKILHRLVGYTSIWERDLRFRLKGEFPENHYIEEIFNFDNSKNVKYKSGQIV
EKYINFYKELYKDNVEKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLE
NLRKLLSYDRKLKNAIMKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKK
LMTDRNSEELCELVKVMFEYKALE

(9) RBD#3#4L
MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNPGAHLTV
KKIFVGGIKEDTEEHHLRDYFEQYGKIEVIEIMTDRGSGKKRGFAFVTFDDHDSVDKIVI
QKYHTVNGHNCEVRKALSKQEMASASSSQRGRSGGSGGSGGSASNVTNKTDPRSMNS
RVFIGNLNTLVVKKSDVEAIFSKYGKIVGCSVHKGFAFVQYVNERNARAAVAGEDGRM
IAGQVLDINLAAEPKVNRGKAGVKRSAAEMYGNKGEEKYVSGEVDKIYNENKQNEVK
ENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNLELEGKDIFAFKNIAPSEISK
KMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNTKFNFVNKNIPFVPSFTKLY
NKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNKFVKNSKVFFKITNEVIKIN
KQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDKEEKNTYIDFIQQIFLKGFID
YLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKNYEKHNRNKEIPHEINEFVR
EIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQSANKEETFSDELELINLLNLD
NNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKIYFDGENIIKHRAFYNIKKYG
MLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQNLHRKYARPKKDEKFNDED
YKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRLVGYTSIWERDLRFRLKGEFP
ENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVKKLKQEKK
DLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYGFVATFKIG
ADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

(10) RBD#4#3L
MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNASNVTNK
TDPRSMNSRVFIGNLNTLVVKKSDVEAIFSKYGKIVGCSVHKGFAFVQYVNERNARAA
VAGEDGRMIAGQVLDINLAAEPKVNRGKAGVKRSAAEMYGSGGSGGSGGSPGAHLTV
KKIFVGGIKEDTEEHHLRDYFEQYGKIEVIEIMTDRGSGKKRGFAFVTFDDHDSVDKIVI
QKYHTVNGHNCEVRKALSKQEMASASSSQRGRNKGEEKYVSGEVDKIYNENKQNEVK
ENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNLELEGKDIFAFKNIAPSEISK
KMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNTKFNFVNKNIPFVPSFTKLY

NKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNKFVKNSKVFFKITNEVIKIN
KQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDKEEKNTYIDFIQQIFLKGFID
YLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKNYEKHNRNKEIPHEINEFVR
EIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQSANKEETFSDELELINLLNLD
NNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKIYFDGENIIKHRAFYNIKKYG
MLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQNLHRKYARPKKDEKFNDED
YKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRLVGYTSIWERDLRFRLKGEFP
ENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVKKLKQEKK
DLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYGFVATFKIG
ADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

<u>Loop 1 N416/K417 fusions</u>

(11) RBD#3 (N416/K417)

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVK**NN**PGAHLT
VKKIFVGGIKEDTEEHHLRDYFEQYGKIEVIEIMTDRGSGKKRGFAFVTFDDHDSVDKIV
IQKYHTVNGHNCEVRKALSKQEMASASSSQRGR**KG**EEKYVSGEVDKIYNENKQNEVK
ENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNLELEGKDIFAFKNIAPSEISK
KMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNTKFNFVNKNIPFVPSFTKLY
NKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNKFVKNSKVFFKITNEVIKIN
KQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDKEEKNTYIDFIQQIFLKGFID
YLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKNYEKHNRNKEIPHEINEFVR
EIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQSANKEETFSDELELINLLNLD
NNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKIYFDGENIIKHRAFYNIKKYG
MLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQNLHRKYARPKKDEKFNDED
YKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRLVGYTSIWERDLRFRLKGEFP
ENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVKKLKQEKK
DLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYGFVATFKIG
ADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

(12) RBD#4 (N416/K417)

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVK**NN**ASNVTN
KTDPRSMNSRVFIGNLNTLVVKKSDVEAIFSKYGKIVGCSVHKGFAFVQYVNERNARA
AVAGEDGRMIAGQVLDINLAAEPKVNRGKAGVKRSAAEMYG**KG**EEKYVSGEVDKIYN
ENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNLELEGKDIFAF

KNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNTKFNFVNKNIP
FVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNKFVKNSKVFFK
ITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDKEEKNTYIDFIQ
QIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKNYEKHNRNKEIP
HEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQSANKEETFSDELE
LINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKIYFDGENIIKHRAF
YNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQNLHRKYARPKKD
EKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRLVGYTSIWERDLR
FRLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVK
KLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYG
FVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

Loop 1 K417/G418 fusions

(13) RBD#3 (K417/G418)

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVK**NNK**PGAHL
TVKKIFVGGIKEDTEEHHLRDYFEQYGKIEVIEIMTDRGSGKKRGFAFVTFDDHDSVDKI
VIQKYHTVNGHNCEVRKALSKQEMASASSSQRGR**G**EEKYVSGEVDKIYNENKQNEVKE
NLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNLELEGKDIFAFKNIAPSEISKK
MFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNTKFNFVNKNIPFVPSFTKLYN
KIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNKFVKNSKVFFKITNEVIKINK
QRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDKEEKNTYIDFIQQIFLKGFIDY
LNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKNYEKHNRNKEIPHEINEFVREI
KLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQSANKEETFSDELELINLLNLDN
NRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKIYFDGENIIKHRAFYNIKKYGM
LNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQNLHRKYARPKKDEKFNDEDY
KEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRLVGYTSIWERDLRFRLKGEFPE
NHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVKKLKQEKKD
LYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYGFVATFKIGA
DKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

(14) RBD#4 (K417/G418)

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVK**NNK**ASNVT
NKTDPRSMNSRVFIGNLNTLVVKKSDVEAIFSKYGKIVGCSVHKGFAFVQYVNERNAR
AAVAGEDGRMIAGQVLDINLAAEPKVNRGKAGVKRSAAEMYG**G**EEKYVSGEVDKIYN

ENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNLELEGKDIFAF
KNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNTKFNFVNKNIP
FVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNKFVKNSKVFFK
ITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDKEEKNTYIDFIQ
QIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKNYEKHNRNKEIP
HEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQSANKEETFSDELE
LINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKIYFDGENIIKHRAF
YNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQNLHRKYARPKKD
EKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRLVGYTSIWERDLR
FRLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVK
KLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYG
FVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

Loop 2 S996/K997 fusions

(15) RBD#3 (S996/K997-no linker)

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKY
VSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNL
ELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNT
KFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNK
FVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDK
EEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKN
YEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQS
ANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKI
YFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQ
NLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRL
VGYTSIWERDLRFRLKGEFPENHYIEEIFNFDN**S**PGAHLTVKKIFVGGIKEDTEEHHLRDY
FEQYGKIEVIEIMTDRGSGKKRGFAFVTFDDHDSVDKIVIQKYHTVNGHNCEVRKALSK
QEMASASSSQRGR**K**NVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVKKLKQEKK
DLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYGFVATFKIG
ADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

(16) RBD#4 (S996/K997-no linker)

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKY
VSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNL

ELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNT
KFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNK
FVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDK
EEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKN
YEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQS
ANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKI
YFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQ
NLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRL
VGYTSIWERDLRFRLKGEFPENHYIEEIFNFDN**S**ASNVTNKTDPRSMNSRVFIGNLNTLV
VKKSDVEAIFSKYGKIVGCSVHKGFAFVQYVNERNARAAVAGEDGRMIAGQVLDINLA
AEPKVNRGKAGVKRSAAEMYG**K**NVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKK
VKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKE
YGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

(17) RBD#3 (S996/K997-shorter linkers)

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKY
VSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNL
ELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNT
KFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNK
FVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDK
EEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKN
YEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQS
ANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKI
YFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQ
NLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRL
VGYTSIWERDLRFRLKGEFPENHYIEEIFNFDN**S**GSSGPGAHLTVKKIFVGGIKEDTEEHH
LRDYFEQYGKIEVIEIMTDRGSGKKRGFAFVTFDDHDSVDKIVIQKYHTVNGHNCEVRK
ALSKQEMASASSSQRGRGSSG**K**NVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKV
KKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEY
GFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

(18) RBD#4 (S996/K997-shorter linkers)

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKY
VSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNL

ELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNT
KFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNK
FVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDK
EEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKN
YEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQS
ANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKI
YFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQ
NLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRL
VGYTSIWERDLRFRLKGEFPENHYIEEIFNFDN**S**GSSGASNVTNKTDPRSMNSRVFIGNL
NTLVVKKSDVEAIFSKYGKIVGCSVHKGFAFVQYVNERNARAAVAGEDGRMIAGQVL
DINLAAEPKVNRGKAGVKRSAAEMYGGSSG**K**NVKYKSGQIVEKYINFYKELYKDNVE
KRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAI
MKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVK
VMFEYKALE

(19) RBD#3 (S996/K997-longer linkers)

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKY
VSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNL
ELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNT
KFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNK
FVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDK
EEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKN
YEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQS
ANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKI
YFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQ
NLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRL
VGYTSIWERDLRFRLKGEFPENHYIEEIFNFDN**S**GGGGSGGGGSGGGGSPGAHLTVKKIF
VGGIKEDTEEHHLRDYFEQYGKIEVIEIMTDRGSGKKRGFAFVTFDDHDSVDKIVIQKYH
TVNGHNCEVRKALSKQEMASASSSQRGRGGGGSGGGGSGGGGS**K**NVKYKSGQIVEKY
INFYKELYKDNVEKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLR
KLLSYDRKLKNAIMKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLM
TDRNSEELCELVKVMFEYKALE

(20) RBD#4 (S996/K997-longer linkers)

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE

IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKY
VSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNL
ELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNT
KFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNK
FVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDK
EEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKN
YEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQS
ANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKI
YFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQ
NLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRL
VGYTSIWERDLRFRLKGEFPENHYIEEIFNFDN**S**GGGGSGGGGSGGGGSASNVTNKTDP
RSMNSRVFIGNLNTLVVKKSDVEAIFSKYGKIVGCSVHKGFAFVQYVNERNARAAVAG
EDGRMIAGQVLDINLAAEPKVNRGKAGVKRSAAEMYGGGGGSGGGGSGGGGS**K**NVK
YKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEI
SLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHL
KNLKKKKLMTDRNSEELCELVKVMFEYKALE

<u>N-terminal Fusions</u>

(21) RBD#1N

MMPNKVRKIGELVRYLNTNPVGGLLEYARSHGFAAEFKLVDQSGPPHEPKFVYQAKVG
GRWFPAVCAHSKKQGKQEAADAALRVLIGENEKAERSGGSSGGSSGSETPGTSESATPE
SSGGSSGGSMKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNA
SEEENRIRRENLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNS
FSVLKKILLNEDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGK
SKRNIIYDYYRESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKI
IGRKNDKENFAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYA
FCHFVEIEMSQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKY
NYYLQVGEIATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVK
NNKGEEKYVSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSI
RHGIVHFNLELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKD
VIIKYLKNTKFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNI
YYGEFLNKFVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSR
EMINNQDKEEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKE
KYDKILKNYEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLK
GSLEKYQSANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKEL
KKFDTNKIYFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIE
KNYTMQQNLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQG
LLLKILHRLVGYTSIWERDLRFRLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYINFY
KELYKDNVEKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLS
YDRKLKNAIMKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRN
SEELCELVKVMFEYKALE

(22) RBD#2N

MSKSESPKEPEQLRKLFIGGLSFETTDESLRSHFEQWGTLTDCVVMRDPNTKRSRGFGFV
TYATVEEVDAAMNARPHKVDGRVVEPKRAVSREDSQRPGAHLTVSGGSSGGSSGSETP
GTSESATPESSGGSSGGSMKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDI

YIKNPDNASEEENRIRRENLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISE
YDLKNKNSFSVLKKILLNEDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINEN
NVEKVGGKSKRNIIYDYYRESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEK
YKIREYYHKIIGRKNDKENFAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKE
ELNDKNIKYAFCHFVEIEMSQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKL
DTYVRNCGKYNYYLQVGEIATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDI
TGRMRGKTVKNNKGEEKYVSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIED
FFANIDEAISSIRHGIVHFNLELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNS
ANVFNYYEKDVIIKYLKNTKFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEE
KDAQIYLLKNIYYGEFLNKFVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTV
PVEYLAIIQSREMINNQDKEEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFS
KIKIKKDNKEKYDKILKNYEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLL
NHKELTNLKGSLEKYQSANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNE
NKIKDRKELKKFDTNKIYFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKE
YSNKKNEIEKNYTMQQNLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEF
NELNLLQGLLLKILHRLVGYTSIWERDLRFRLKGEFPENHYIEEIFNFDNSKNVKYKSGQI
VEKYINFYKELYKDNVEKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVL
ENLRKLLSYDRKLKNAIMKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKK
KLMTDRNSEELCELVKVMFEYKALE

(23) RBD#3N

PGAHLTVKKIFVGGIKEDTEEHHLRDYFEQYGKIEVIEIMTDRGSGKKRGFAFVTFDDHD
SVDKIVIQKYHTVNGHNCEVRKALSKQEMASASSSQRGRSGGSSGGSSGSETPGTSESA
TPESSGGSSGGSMKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPD
NASEEENRIRRENLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNK
NSFSVLKKILLNEDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVG
GKSKRNIIYDYYRESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYY
HKIIGRKNDKENFAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNI
KYAFCHFVEIEMSQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNC
GKYNYYLQVGEIATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRG
KTVKNNKGEEKYVSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDE
AISSIRHGIVHFNLELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNY
YEKDVIIKYLKNTKFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIY
LLKNIYYGEFLNKFVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLA
IIQSREMINNQDKEEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKK
DNKEKYDKILKNYEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKEL
TNLKGSLEKYQSANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKD
RKELKKFDTNKIYFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKK
NEIEKNYTMQQNLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNL
LQGLLLKILHRLVGYTSIWERDLRFRLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYI
NFYKELYKDNVEKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRK
LLSYDRKLKNAIMKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMT
DRNSEELCELVKVMFEYKALE

(24) RBD#4N

ASNVTNKTDPRSMNSRVFIGNLNTLVVKKSDVEAIFSKYGKIVGCSVHKGFAFVQYVNE
RNARAAVAGEDGRMIAGQVLDINLAAEPKVNRGKAGVKRSAAEMYGSGGSSGGSSGS
ETPGTSESATPESSGGSSGGSMKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSI
RLDIYIKNPDNASEEENRIRRENLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEE
DISEYDLKNKNSFSVLKKILLNEDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKI
NENNVEKVGGKSKRNIIYDYYRESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKK
HEKYKIREYYHKIIGRKNDKENFAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYL
DKEELNDKNIKYAFCHFVEIEMSQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLL
NKLDTYVRNCGKYNYYLQVGEIATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETEN
ENDITGRMRGKTVKNNKGEEKYVSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKN
EIEDFFANIDEAISSIRHGIVHFNLELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFK
QLNSANVFNYYEKDVIIKYLKNTKFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPK
DKEEKDAQIYLLKNIYYGEFLNKFVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENI
EKTVPVEYLAIIQSREMINNQDKEEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDN
NDIFSKIKIKKDNKEKYDKILKNYEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYL
ILKLLNHKELTNLKGSLEKYQSANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFL
DFNENKIKDRKELKKFDTNKIYFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLK
ELKEYSNKKNEIEKNYTMQQNLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKN
KVEFNELNLLQGLLLKILHRLVGYTSIWERDLRFRLKGEFPENHYIEEIFNFDNSKNVKY
KSGQIVEKYINFYKELYKDNVEKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEIS
LLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLK
NLKKKKLMTDRNSEELCELVKVMFEYKALE

(25) RBD#5N

SIVEKFRSRGRAQVQEFCDYGTKEECMKASDADRPCRKLHFRRIINKHTDESLGDCSFLN
TCFHMDTCKYVHYEIDACMDSEAPGSKDHTPSQELALTQSGGSSGGSSGSETPGTSESA
TPESSGGSSGGSMKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPD
NASEEENRIRRENLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNK
NSFSVLKKILLNEDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVG
GKSKRNIIYDYYRESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYY
HKIIGRKNDKENFAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNI
KYAFCHFVEIEMSQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNC
GKYNYYLQVGEIATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRG
KTVKNNKGEEKYVSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDE
AISSIRHGIVHFNLELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNY
YEKDVIIKYLKNTKFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIY
LLKNIYYGEFLNKFVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLA
IIQSREMINNQDKEEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKK
DNKEKYDKILKNYEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKEL
TNLKGSLEKYQSANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKD
RKELKKFDTNKIYFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKK
NEIEKNYTMQQNLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNL
LQGLLLKILHRLVGYTSIWERDLRFRLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYI
NFYKELYKDNVEKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRK
LLSYDRKLKNAIMKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMT
DRNSEELCELVKVMFEYKALE

(26) RBD#6N

LSSHFQELSIYQDQEQRILKFLEELGEGKATTAHDLSGKLGTPKKEINRVLYSLAKKGKL
QKEAGTPPLWKIAVSTQSGGSSGGSSGSETPGTSESATPESSGGSSGGSMKVTKVDGISH
KKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRENLKKFFSNKVL
HLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLNEDVNSEELEIFR
KDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYYRESAKRNDYIN
NVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKENFAKIIYEEIQNV
NNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEMSQLLKNYVYKR
LSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGEIATSDFIARNRQ
NEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKYVSGEVDKIYNE
NKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNLELEGKDIFAFK
NIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNTKFNFVNKNIPF
VPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNKFVKNSKVFFKI
TNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDKEEKNTYIDFIQQ
IFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKNYEKHNRNKEIPH
EINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQSANKEETFSDELEL
INLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKIYFDGENIIKHRAFY
NIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQNLHRKYARPKKDE
KFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRLVGYTSIWERDLRF
RLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVKK
LKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYGF
VATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

(27) RBD#7N

FLDMAEIKEKICDYLFNVSDSSALNLAKNIGLTKARDINAVLIDMERQGDVYRQGTTPPI
WHLTDKKRERMQIKSGGSSGGSSGSETPGTSESATPESSGGSSGGSMKVTKVDGISHKK
YIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRENLKKFFSNKVLHL
KDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLNEDVNSEELEIFRK
DVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYYRESAKRNDYINN
VQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKENFAKIIYEEIQNVN
NIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEMSQLLKNYVYKRL
SNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGEIATSDFIARNRQN
EAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKYVSGEVDKIYNEN
KQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNLELEGKDIFAFKNI
APSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNTKFNFVNKNIPFVP
SFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNKFVKNSKVFFKITN
EVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDKEEKNTYIDFIQQIF
LKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKNYEKHNRNKEIPHE
INEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQSANKEETFSDELELI
NLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKIYFDGENIIKHRAFY
NIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQNLHRKYARPKKDE
KFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRLVGYTSIWERDLRF
RLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNVEKRSIYSDKKVKK
LKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAIMKSIVDILKEYGF
VATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVKVMFEYKALE

C-terminal Fusions

(28) RBD#1C

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKY
VSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNL
ELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNT
KFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNK
FVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDK
EEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKN
YEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQS
ANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKI
YFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQ
NLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRL
VGYTSIWERDLRFRLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNV
EKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAI
MKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVK
VMFEYKALESGGSSGGSSGSETPGTSESATPESSGGSSGGSMMPNKVRKIGELVRYLNT
NPVGGLLEYARSHGFAAEFKLVDQSGPPHEPKFVYQAKVGGRWFPAVCAHSKKQGKQ
EAADAALRVLIGENEKAER

(29) RBD#2C

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKY
VSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNL
ELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNT
KFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNK
FVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDK
EEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKN
YEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQS
ANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKI
YFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQ
NLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRL
VGYTSIWERDLRFRLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNV
EKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAI
MKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVK

VMFEYKALESGGSSGGSSGSETPGTSESATPESSGGSSGGSMSKSESPKEPEQLRKLFIGG
LSFETTDESLRSHFEQWGTLTDCVVMRDPNTKRSRGFGFVTYATVEEVDAAMNARPHK
VDGRVVEPKRAVSREDSQRPGAHLTV

(30) RBD#3C

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKY
VSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNL
ELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNT
KFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNK
FVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDK
EEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKN
YEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQS
ANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKI
YFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQ
NLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRL
VGYTSIWERDLRFRLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNV
EKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAI
MKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVK
VMFEYKALESGGSSGGSSGSETPGTSESATPESSGGSSGGSPGAHLTVKKIFVGGIKEDTE
EHHLRDYFEQYGKIEVIEIMTDRGSGKKRGFAFVTFDDHDSVDKIVIQKYHTVNGHNCE
VRKALSKQEMASASSSQRGR

(31) RBD#4C

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKY
VSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNL
ELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNT
KFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNK
FVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDK
EEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKN
YEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQS
ANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKI
YFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQ
NLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRL
VGYTSIWERDLRFRLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNV

EKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAI
MKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVK
VMFEYKALESGGSSGGSSGSETPGTSESATPESSGGSSGGSASNVTNKTDPRSMNSRVFI
GNLNTLVVKKSDVEAIFSKYGKIVGCSVHKGFAFVQYVNERNARAAVAGEDGRMIAG
QVLDINLAAEPKVNRGKAGVKRSAAEMYG

(32) RBD#5C

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKY
VSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNL
ELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNT
KFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNK
FVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDK
EEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKN
YEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQS
ANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKI
YFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQ
NLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRL
VGYTSIWERDLRFRLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNV
EKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAI
MKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVK
VMFEYKALESGGSSGGSSGSETPGTSESATPESSGGSSGGSSIVEKFRSRGRAQVQEFCD
YGTKEECMKASDADRPCRKLHFRRIINKHTDESLGDCSFLNTCFHMDTCKYVHYEIDAC
MDSEAPGSKDHTPSQELALTQ

(33) RBD#6C

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKY
VSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNL
ELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNT
KFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNK
FVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDK
EEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKN
YEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQS
ANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKI
YFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQ

NLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRL
VGYTSIWERDLRFRLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNV
EKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAI
MKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVK
VMFEYKALESGGSSGGSSGSETPGTSESATPESSGGSSGGSLSSHFQELSIYQDQEQRILK
FLEELGEGKATTAHDLSGKLGTPKKEINRVLYSLAKKGKLQKEAGTPPLWKIAVSTQ

(34) RBD#7C

MKVTKVDGISHKKYIEEGKLVKSTSEENRTSERLSELLSIRLDIYIKNPDNASEEENRIRRE
NLKKFFSNKVLHLKDSVLYLKNRKEKNAVQDKNYSEEDISEYDLKNKNSFSVLKKILLN
EDVNSEELEIFRKDVEAKLNKINSLKYSFEENKANYQKINENNVEKVGGKSKRNIIYDYY
RESAKRNDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYHKIIGRKNDKEN
FAKIIYEEIQNVNNIKELIEKIPDMSELKKSQVFYKYYLDKEELNDKNIKYAFCHFVEIEM
SQLLKNYVYKRLSNISNDKIKRIFEYQNLKKLIENKLLNKLDTYVRNCGKYNYYLQVGE
IATSDFIARNRQNEAFLRNIIGVSSVAYFSLRNILETENENDITGRMRGKTVKNNKGEEKY
VSGEVDKIYNENKQNEVKENLKMFYSYDFNMDNKNEIEDFFANIDEAISSIRHGIVHFNL
ELEGKDIFAFKNIAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYEKDVIIKYLKNT
KFNFVNKNIPFVPSFTKLYNKIEDLRNTLKFFWSVPKDKEEKDAQIYLLKNIYYGEFLNK
FVKNSKVFFKITNEVIKINKQRNQKTGHYKYQKFENIEKTVPVEYLAIIQSREMINNQDK
EEKNTYIDFIQQIFLKGFIDYLNKNNLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKN
YEKHNRNKEIPHEINEFVREIKLGKILKYTENLNMFYLILKLLNHKELTNLKGSLEKYQS
ANKEETFSDELELINLLNLDNNRVTEDFELEANEIGKFLDFNENKIKDRKELKKFDTNKI
YFDGENIIKHRAFYNIKKYGMLNLLEKIADKAKYKISLKELKEYSNKKNEIEKNYTMQQ
NLHRKYARPKKDEKFNDEDYKEYEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRL
VGYTSIWERDLRFRLKGEFPENHYIEEIFNFDNSKNVKYKSGQIVEKYINFYKELYKDNV
EKRSIYSDKKVKKLKQEKKDLYIRNYIAHFNYIPHAEISLLEVLENLRKLLSYDRKLKNAI
MKSIVDILKEYGFVATFKIGADKKIEIQTLESEKIVHLKNLKKKKLMTDRNSEELCELVK
VMFEYKALESGGSSGGSSGSETPGTSESATPESSGGSSGGSFLDMAEIKEKICDYLFNVSD
SSALNLAKNIGLTKARDINAVLIDMERQGDVYRQGTTPPIWHLTDKKRERMQIK

2. Target RNA sequences

Target ID	Sequence (5'→3')	Description	Related Figures
T1_N[4]	gucugauaauggaccccaaaaucagcgaaaugcaccccgcauuacguuugguggacccucagauucaacuggcaguaaccagaauggagaacgcagugggggcgcg	SARS-CoV-2 (Ref Seq: NC_045512.2) N gene fragment: 28,276–28,380	Fig. 1b, 1c, 2d, 2g, 3, 5a, and 6a–6c; Extended Data Fig. 1b, 1c, 2g, 2h, 3, 4, 5c–5f, 6, 7a, 7b, 8a, and 9; Fig. S1– S3, S5, S9, and S10b.
T2_RdRp[5]	gugauagagccaugccuaacaugcuuagaauuauggccucacuuguucuugcucgcaaacauacaacguguuguagcuugucacaccguuucuauagauuagcuaaugaguguguccaaguauugaguguaaauggucaugugugggcgguucacuauauguuaaaccagguggaaccucaucaggagaugccacaacugcuuaugcuaauaguguuuuuuaacauuugu	SARS-CoV-2 (Ref Seq: NC_045512.2) RdRp gene fragment: 15,305–15,531	Extended Data Fig. 2a, 2c, 2d, and 2f.
T3_ssRNA1[6]	ggccagugaauucgagcucgguacccgggggauccucuagaaauauggauuacuugguagaacagcaaucuacucgaccugcaggcaugcaagcuuggcguaaucauggucauagcuguuuccuguguuuauccgcucacaauuccacacaacauacgagccggaagcauaaag	Artificial RNA sequence	Fig. 4a, 4b; Extended Data Fig. 2b, 2c, 2e, and 2f; Fig. S4a
T4_N_PM	cgcauuacguuugguggacccucagauu	SARS-CoV-2 (Ref Seq: NC_045512.2) N gene fragment: 28,313–28,340	Fig. 4c; Fig. S4b.
T5_N_MM2	cCcauuacguuugguggacccucagauu	single mismatch at 2nd position	Fig. 4c; Fig. S4b.
T6_N_MM6	cgcauAacguuugguggacccucagauu	single mismatch at 6th position	Fig. 4c; Fig. S4b.
T7_N_MM10	cgcauuacgCuugguggacccucagauu	single mismatch at 10th position	Fig. 4c; Fig. S4b.
T8_N_MM14	cgcauuacguuugCuggacccucagauu	single mismatch at 14th position	Fig. 4c; Fig. S4b.
T9_N_MM18	cgcauuacguuuggugUcccucagauu	single mismatch at 18th position	Fig. 4c; Fig. S4b.

Target ID	Sequence (5'→3')	Description	Related Figures
T10_N_MM22	cgcauuacguuugguggacccAcagauu	single mismatch at 22nd position	Fig. 4c; Fig. S4b.
T11_N_MM26	cgcauuacguuugguggacccucagUuu	single mismatch at 26th position	Fig. 4c; Fig. S4b.
T12_N_MM4	cgcUuuacguuugguggacccucagauu	single mismatch at 4th position	Fig. 4c; Fig. S4b.
T13_N_MM8	cgcauuaGguuugguggacccucagauu	single mismatch at 8th position	Fig. 4c; Fig. S4b.
T14_N_MM12	cgcauuacguuAgguggacccucagauu	single mismatch at 12th position	Fig. 4c; Fig. S4b.
T15_N_MM16	cgcauuacguuugguCgacccucagauu	single mismatch at 16th position	Fig. 4c; Fig. S4b.
T16_N_MM20	cgcauuacguuugguggacGcucagauu	single mismatch at 20th position	Fig. 4c; Fig. S4b.
T17_N_MM24	cgcauuacguuugguggacccucUgauu	single mismatch at 24th position	Fig. 4c; Fig. S4b.
T18_N_MM28	cgcauuacguuugguggacccucagauA	single mismatch at 28th position	Fig. 4c; Fig. S4b.
T19_N_DM1	GCcauuacguuugguggacccucagauu	consecutive double mismatch at 1st and 2nd positions	Fig. 4c; Fig. S4b.
T20_N_DM5	cgcaAAacguuugguggacccucagauu	consecutive double mismatch at 5th and 6th positions	Fig. 4c; Fig. S4b.
T21_N_DM9	cgcauuacCAuugguggacccucagauu	consecutive double mismatch at 9th and 10th positions	Fig. 4c; Fig. S4b.
T22_N_DM13	cgcauuacguuuCCuggacccucagauu	consecutive double mismatch at 13th and 14th positions	Fig. 4c; Fig. S4b.
T23_N_DM17	cgcauuacguuugguCUcccucagauu	consecutive double mismatch at 17th and 18th positions	Fig. 4c; Fig. S4b.
T24_N_DM21	cgcauuacguuugguggaccGAcagauu	consecutive double mismatch at 21st and 22nd positions	Fig. 4c; Fig. S4b.

Target ID	Sequence (5'→3')	Description	Related Figures
T25_N_DM25	cgcauuacguuugguggacccucaCUuu	consecutive double mismatch at 25th and 26th positions	Fig. 4c; Fig. S4b.
T26_N_2[4]	accccgcauuacguuugguggacccucagauucaac	SARS-CoV-2 (Ref Seq: NC_045512.2) N gene fragment: 28,309–28,344	Extended Data Fig. 5a, 5b.
T27_Zika[6]	agcuggaguguuguuugguaugggcaaaggaugccauucuacgcaugggacuuuggagucccgcugcuaaugauagguugcuacucacaauuaacaccccugacccuaauaguggccaucauuuugcucguggcgcacuacauguacuugaucccagggcugcaggcagcagcugcgcgugcugcccagaagagaacggcagcuggcaucaugaagaacccuguuguggaugggaauaguggugacugacauugacacaaugacaauugacccccaaguggagaaaaagauggacaggugcuacucauagcaguagcagucuccagcgccaua	Zika virus (Ref Seq: NC_035889.1) POLY gene fragment: 7,133–7,466	Fig.5b; Extended Data Fig. 7c and 8b.
T28_Dengue[6]	aguacauauucaggggccaaccucucaacaaugacgaagaccaugcucacuggacagaagcaaaaaugcugcuggacaacaucaacacaccagaagggauuauaccagcucucuuugaaccagaaagggagaagucagccgccauagacggugaauaccgccugaagggu	Dengue virus type 3 strain CH53489 (GenBank: DQ863638.1) POLY gene fragment: 5,928–6,097	Fig. 5c; Extended Data Fig. 7d and 8c.
T29_Ebola[7]	gaggaaaauaacauugcaaagguggagccuaugguuuaguuaucuugaucauugugauaauauccuggcggaggcuuuaacccaaauaacuugcacaguugauuuagcacagauucugagggaauauucaugggcucauauuuuagagggaagaccucuuauuggagccacac	Ebola virus (Ref seq: NC_002549.1) L gene fragment: 14,802–14,974	Fig. 5d; Extended Data Fig. 7e and 8d.
T30_miR19b	ugugcaaauccaugcaaaacuga	ID: hsa-miR-19b-3p (Accession: MIMAT0000074)	Fig. 5e; Extended Data Fig.7f and 7g.
T31_miR2392	uaggaugggggugagaggug	ID: hsa-miR-2392 (Accession: MIMAT0019043)	Fig. 5f; Extended Data Fig. 7h–7j.

Notes:

a. Protospacers are underlined.
b. MISMATCHES are in upper cases.
c. T1–T29 were obtained by IVT and gel-purified (T1–T3 and T26–T29) or magnetic bead-purified (T4–T25). T30 and T31 were ordered from IDT.

3. CRISPR RNA (crRNA) sequences

crRNA ID	Sequence (5'→3')	Description	Related Figures
cr1_N[4]	GACUACCCCAAAAACGAAGGGGACUAAAACaaucuggaggguccaccaaacguaaugcg	targeting T1_N	Fig. 1b, 1c, 2d, 2g, 3, 4c, 5a and 6a–6i; Extended Data Fig. 1b, 1c, 2g, 2h, 3–6, 7a, 7b, 8a and 9. Fig. S1–S3, S4b, S5, and S9.
cr2_RdRp[5]	GACTACCCCAAAAACGAAGGGGACTAAAACtcactcaatacttgagcacactcattag	targeting T3_RdRp	Extended Data Fig. 2a, 2c, 2d and 2f.
cr3_ssRNA1_0[6]	GACUACCCCAAAAACGAAGGGGACUAAAACuagauugcuguucuaccaaguaauccau	targeting T2_ssRNA1	Extended Data Fig. 2b, 2c, 2e and 2f.
cr4_ssRNA1_1[8]	GACUACCCCAAAAACGAAGGGGACUAAAACccggguaccgagcucgaauucacuggcc	targeting T2_ssRNA1	Fig. 4a and 4b; Fig. S4a
cr5_ssRNA1_2[8]	GACUACCCCAAAAACGAAGGGGACUAAAACuuucuagaggaucccggguaccgagcu	targeting T2_ssRNA1	Fig. 4a and 4b; Fig. S4a
cr6_ssRNA1_3[8]	GACUACCCCAAAAACGAAGGGGACUAAAACccaaguaauccauauuucuagaggaucc	targeting T2_ssRNA1	Fig. 4a and 4b; Fig. S4a
cr7_ssRNA1_4[8]	GACUACCCCAAAAACGAAGGGGACUAAAACagauugcuguucuaccaaguaauccaua	targeting T2_ssRNA1	Fig. 4a and 4b; Fig. S4a
cr8_ssRNA1_5[8]	GACUACCCCAAAAACGAAGGGGACUAAAACccugcaggucgaguagauugcuguucua	targeting T2_ssRNA1	Fig. 4a and 4b; Fig. S4a
cr9_ssRNA1_6[8]	GACUACCCCAAAAACGAAGGGGACUAAAACgccaagcuugcaugccugcaggucgagu	targeting T2_ssRNA1	Fig. 4a and 4b; Fig. S4a
cr10_ssRNA1_7[8]	GACUACCCCAAAAACGAAGGGGACUAAAACaugaccaugauuacgccaagcuugcaug	targeting T2_ssRNA1	Fig. 4a and 4b; Fig. S4a
cr11_ssRNA1_8[8]	GACUACCCCAAAAACGAAGGGGACUAAAACcacaggaaacagcuaugaccaugauuac	targeting T2_ssRNA1	Fig. 4a and 4b; Fig. S4a
cr12_ssRNA1_9[8]	GACUACCCCAAAAACGAAGGGGACUAAAACugugagcggauaaacacaggaaacagcu	targeting T2_ssRNA1	Fig. 4a and 4b; Fig. S4a

crRNA ID	Sequence (5'→3')	Description	Related Figures
cr13_ssRNA1_10[8]	GACUACCCCAAAAACGAAGGGGACUAAAACauguugugguggaauugugagcggauaaa	targeting T2_ssRNA1	Fig. 4a and 4b; Fig. S4a
cr14_ssRNA1_11[8]	GACUACCCCAAAAACGAAGGGGACUAAAACugcuuccggcucguauguuguguggaau	targeting T2_ssRNA1	Fig. 4a and 4b; Fig. S4a
cr15_Zika[6]	GACUACCCCAAAAACGAAGGGGACUAAAACcauguagugcgccacgagcaaaaugaug	targeting T19_Zika	Fig. 5b; Extended Data Fig. 7c and 8b
cr16_Dengue[6]	GACUACCCCAAAAACGAAGGGGACUAAAACgguauaaucccuucuggugugguugaugu	targeting T20_Dengue	Fig. 5c; Extended Data Fig. 7d and 8c
cr17_Ebola[7]	GACUACCCCAAAAACGAAGGGGACUAAAACaucaacugugcaaguuauuuggguuaaa	targeting T21_Ebola	Fig. 5d; Extended Data Fig. 7e and 8d
cr18_miR19b	GACUACCCCAAAAACGAAGGGGACUAAAACucaguuuugcauggauuugcaca	targeting T22_miR19b	Fig.5e; Extended Data Fig. 7f and 7g
cr19_miR2392	GACUACCCCAAAAACGAAGGGGACUAAAACcaccucucaccccccauccua	targeting T23_miR2392	Fig. 5f; Extended Data Fig. 7h–7j

Note:

a. 5' Direct repeat is in upper case, and spacer is in lower case.
b. cr1–cr3 were ordered from Synthego. cr4–cr1929 were obtained by IVT and gel-purified.

4. Reporter RNA oligonucleotide sequences

reporter ID	Sequence (5'→3')	Source	Related Figures
r1_FU5Q	/56-FAM/rUrUrUrUrU/3IABkFQ/	Ordered oligos (IDT)	Fig. 3c and 3d
r2_FU5	/56-FAM/rUrUrUrUrU	Ordered oligos (IDT)	Fig. 3a and 3b; Extended Data Fig. 3
r3_FU11Q	/56-FAM/rUrUrUrUrUrUrUrUrUrU/3IABkFQ/	Ordered oligos (IDT)	Fig. 3c, 3d, 4 and 5 Extended Data Fig. 2d–2h, 4 and 6–8 Fig. S1–S3 and S5
r4_FU11	/56-FAM/rUrUrUrUrUrUrUrUrUrUrU	Ordered oligos (IDT)	Fig. 3a and 3b; Extended Data Fig. 3
r5_FU15	/56-FAM/rUrUrUrUrUrUrUrUrUrUrUrUrUrU	Ordered oligos (IDT)	Fig. 3a and 3b; Extended Data Fig. 3
r6_FU20	/56-FAM/rUrUrUrUrUrUrUrUrUrUrUrUrUrUrUrUrUrU	Ordered oligos (IDT)	Fig. 3a and 3b; Extended Data Fig. 3, 5e and 5f.
r7_MBU20	/5ThioMC6-D/rUrUrUrUrUrUrUrUrUrUrUrUrUrUrUrUrUrU/3MeBlN/	Ordered oligos (IDT, GeneLink)	IDT: Figure 6a–6f; Extended Data Fig. 9; Fig. S8. GeneLink: Figure 6g–i; Fig. S9
RNaseAlert	$(N)_7$	IDT (Cat. 11-02-01-02)	Fig. 1b, 1c, 2d, 2g, 3c and 3d Extended Data Fig. 1b, 1c and 2a–2c.

Notes:
/56-FAM/: 5' 6-FAM (carboxyfluorescein)
/3IABkFQ/: 3' Iowa Black quencher
/5ThioMC6-D/: 5' Thiol Modifier C6 S–S modification
/3MeBlN/: 3' Methylene blue

5. IVT Primers

Primer ID	Sequences (5'→3')
Pr01_cr_univ_F	GAAATTAATACGACTCACTATAGGGACTACCCCAAAAACG AAGGGGACTAAAAC
Pr02_cr4_ssRNA1_R1	GGCCAGTGAATTCGAGCTCGGTACCCGGGTTTTAGTCCCCT TCGTTTTTGGGGT
Pr03_cr5_ssRNA1_R2	AGCTCGGTACCCGGGGATCCTCTAGAAAGTTTTAGTCCCCT TCGTTTTTGGGGT
Pr04_cr6_ssRNA1_R3	GGATCCTCTAGAAATATGGATTACTTGGGTTTTAGTCCCCT TCGTTTTTGGGGT
Pr05_cr7_ssRNA1_R4	TATGGATTACTTGGTAGAACAGCAATCTGTTTTAGTCCCCT TCGTTTTTGGGGT
Pr06_cr8_ssRNA1_R5	TAGAACAGCAATCTACTCGACCTGCAGGGTTTTAGTCCCCT TCGTTTTTGGGGT
Pr07_cr9_ssRNA1_R6	ACTCGACCTGCAGGCATGCAAGCTTGGCGTTTTAGTCCCCT TCGTTTTTGGGGT
Pr08_cr10_ssRNA1_R7	CATGCAAGCTTGGCGTAATCATGGTCATGTTTTAGTCCCCT TCGTTTTTGGGGT
Pr09_cr11_ssRNA1_R8	GTAATCATGGTCATAGCTGTTTCCTGTGGTTTTAGTCCCCT TCGTTTTTGGGGT
Pr10_cr12_ssRNA1_R9	AGCTGTTTCCTGTGTTTATCCGCTCACAGTTTTAGTCCCCTT CGTTTTTGGGGT
Pr11_cr13_ssRNA1_R10	TTTATCCGCTCACAATTCCACACAACATGTTTTAGTCCCCT TCGTTTTTGGGGT
Pr12_cr14_ssRNA1_R11	ATTCCACACAACATACGAGCCGGAAGCAGTTTTAGTCCCC TTCGTTTTTGGGGT
Pr13_cr15_Zika_R	CATCATTTTGCTCGTGGCGCACTACATGGTTTTAGTCCCCT TCGTTTTTGGGGT

Primer ID	**Sequences (5'→3')**
Pr14_cr16_Dengue_R	ACATCAACACACCAGAAGGGATTATACCGTTTTAGTCCCCTTCGTTTTTGGGGT
Pr15_cr17_Ebola_R	TTTAACCCAAATAACTTGCACAGTTGATGTTTTAGTCCCCTTCGTTTTTGGGGT
Pr16_cr18_miR19b_R	TGTGCAAATCCATGCAAAACTGAGTTTTAGTCCCCTTCGTTTTTGGGGT
Pr17_cr19_miR2392_R	TAGGATGGGGGTGAGAGGTGGTTTTAGTCCCCTTCGTTTTTGGGGT
Pr18_Tar_3G_F	GAAATTAATACGACTCACTATAGGG
Pr19_T1_N_R	CGCGCCCCACTGCGTTCTCC
Pr20_T2_ssRNA1_R	CTTTATGCTTCCGGCTCGTA
Pr21_T3_RdRp_R	ACAAATGTTAAAAACACTATTAGCATAA
Pr22_T4-18_T20-25_F	GAAATTAATACGACTCACTATAGGC
Pr23_T4_R	AATCTGAGGGTCCACCAAACGTAATGCGCCTATAGTGAGTCGTATTAATTTC
Pr24_T5_R	AATCTGAGGGTCCACCAAACGTAATGGGCCTATAGTGAGTCGTATTAATTTC
Pr25_T6_R	AATCTGAGGGTCCACCAAACGTTATGCGCCTATAGTGAGTCGTATTAATTTC
Pr26_T7_R	AATCTGAGGGTCCACCAAGCGTAATGCGCCTATAGTGAGTCGTATTAATTTC
Pr27_T8_R	AATCTGAGGGTCCAGCAAACGTAATGCGCCTATAGTGAGTCGTATTAATTTC
Pr28_T9_R	AATCTGAGGGACCACCAAACGTAATGCGCCTATAGTGAGTCGTATTAATTTC
Pr29_T10_R	AATCTGTGGGTCCACCAAACGTAATGCGCCTATAGTGAGTCGTATTAATTTC
Pr30_T11_R	AAACTGAGGGTCCACCAAACGTAATGCGCCTATAGTGAGTCGTATTAATTTC

Primer ID	**Sequences (5'→3')**
Pr31_T12_R	AATCTGAGGGTCCACCAAACGTAAAGCGCCTATAGTGAGT CGTATTAATTTC
Pr32_T13_R	AATCTGAGGGTCCACCAAACCTAATGCGCCTATAGTGAGT CGTATTAATTTC
Pr33_T14_R	AATCTGAGGGTCCACCTAACGTAATGCGCCTATAGTGAGT CGTATTAATTTC
Pr34_T15_R	AATCTGAGGGTCGACCAAACGTAATGCGCCTATAGTGAGT CGTATTAATTTC
Pr35_T16_R	AATCTGAGCGTCCACCAAACGTAATGCGCCTATAGTGAGT CGTATTAATTTC
Pr36_T17_R	AATCAGAGGGTCCACCAAACGTAATGCGCCTATAGTGAGT CGTATTAATTTC
Pr37_T18_R	TATCTGAGGGTCCACCAAACGTAATGCGCCTATAGTGAGT CGTATTAATTTC
Pr38_T19_R	AATCTGAGGGTCCACCAAACGTAATGGCCCTATAGTGAGT CGTATTAATTTC
Pr39_T20_R	AATCTGAGGGTCCACCAAACGTTTTGCGCCTATAGTGAGT CGTATTAATTTC
Pr40_T21_R	AATCTGAGGGTCCACCAATGGTAATGCGCCTATAGTGAGT CGTATTAATTTC
Pr41_T22_R	AATCTGAGGGTCCAGGAAACGTAATGCGCCTATAGTGAGT CGTATTAATTTC
Pr42_T23_R	AATCTGAGGGAGCACCAAACGTAATGCGCCTATAGTGAGT CGTATTAATTTC
Pr43_T24_R	AATCTGTCGGTCCACCAAACGTAATGCGCCTATAGTGAGT CGTATTAATTTC
Pr44_T25_R	AAAGTGAGGGTCCACCAAACGTAATGCGCCTATAGTGAGT CGTATTAATTTC

Primer ID	**Sequences (5'→3')**
Pr45_T26_N_2_F	GAAATTAATACGACTCACTATAGGACCCCGCATTACGTTTGGTGGACCCTCAGATTCAAC
Pr46_T26_N_2_R	GTTGAATCTGAGGGTCCACCAAACGTAATGCGGGGTCCTATAGTGAGTCGTATTAATTTC
Pr47_T27_Zika_R	TATGGCGCTGGAGACTGCTACT
Pr48_T28_Dengue_F	GAAATTAATACGACTCACTATAGGGAGTACATATTCAGGGGCCAACCT
Pr49_T28_Dengue_R	ACCCTTCAGGCGGTATTCACC
Pr50_T29_Ebola_F	GAAATTAATACGACTCACTATAGGGGAGGAAAATAACATTGCAAAGGTGGAG
Pr51_T29_Ebola_R	GTGTGGCTCCAATAAGAGGTCTTC

6. Cloning Primers

Primer ID	Name	Sequences (5'→3')
Loo1 1 Fusion		
CP001	P1_RBD_F	TCTCAGGGTCTCGGTGGATCTCGCGGTATCATTGCAG A
CP002	P1_RBD_R	TCTCAGGGTCTCGTTCACGGTCTTGCCCCGCATC
CP003	P2_RBD1_F	TCTCAGGGTCTCGTGAAGAACATGATGCCCAACAAGC TCAGG
CP004	P2_RBD1_R	TCTCAGGGTCTCGCCTTGTTGCGTTCTGCCTTCTCGTT T
CP005	P2_RBD2_F	TCTCAGGGTCTCCTGAAGAACATGTCTAAGTCAGAGT TCCTAAAGAGC
CP006	P2_RBD2_R	TCTCAGGGTCTCCCCTTGTTCACAGTTAAGTGGGCAC TGG
CP007	P2_RBD3_F	TCTCAGGGTCTCGTGAAGAACCCAGGTGCCCACTTAA CTGTG
CP008	P2_RBD3_R	TCTCAGGGTCTCGCCTTGTTTTCGACCTCTTTGGCTGG ATG
CP009	P2_RBD4_F	TCTCAGGGTCTCCTGAAGAACGCCAGCAACGTTACCA ACAAGA
CP010	P2_RBD4_R	TCTCAGGGTCTCCCCTTGTTCCCGTACATCTCCGCTGC AG
CP011	P2_RBD5_F	TCTCAGGGTCTCCTGAAGAACTCCATTGTTGAAAAAT TCGCTCTCGA
CP012	P2_RBD5_R	TCTCAGGGTCTCCCCTTGTTCTGTGTAAGAGCAAGCTC CTGG
CP013	P2_RBD6_F	TCTCAGGGTCTCCTGAAGAACCTTTCCTCACATTTCCA GGAACTGAG
CP014	P2_RBD6_R	TCTCAGGGTCTCCCCTTGTTCTGAGTGGAAACCGCGA TTTCC

Primer ID	Name	Sequences (5'→3')
CP015	P2_RBD7_F	TCTCAGGGTCTCCTGAAGAACTTTTTAGACATGGCCG GATCAAGG
CP016	P2_RBD7_R	TCTCAGGGTCTCCCCTTGTTCTTGATTTGCATCCTCTC CGCTT
CP017	RBD34_cDNA_F	ACTTCGACCTCTTTGGCTGG
CP018	RBD34_cDNA_R	TCAGCTTGCTCCTTTCTGCC
CP019	P3_RBD_F	TCTCAGGGTCTCGAAGGGCGAAGAGAAATACGTGTC G
CP020	P3_RBD_R	TCTCAGGGTCTCGCCACGCTCACCGGCTCCAGATT
C- and N-terminal Fusion		
CP021	P1_RBD3C_F	CGCATTGGTCTCCGCGTGGATCTCGCGGTATCATTGC
CP022	P1_RBD3C_R	CGCATTGGTCTCCTCATGGATCCACCAATCTGTTCTCT GTGAGC
CP023	P2_RBD3C_F	CGCATTGGTCTCCATGAAAGTGACCAAGGTCGACGG
CP024	P2_RBD3C_R	CGCATTGGTCTCCACCGCCGCTGCTGCCACCGCTTTCC AGGGCCTTGTACTCGAAC
CP025	P3_RBD3C_T	CGGTAGCTCCGGTAGCGAAACACCGGGGACTTCAGAA TCGGCCACACCGGAGTCTAGCG
CP026	P3_RBD3C_B	CCACCGCTAGACTCCGGTGTGGCCGATTCTGAAGTCC CGGTGTTTCGCTACCGGAGCT
CP027	P4_RBD3C_F	CGCATTGGTCTCCGTGGCAGCAGCGGCGGTAGCCCAC GTGCCCACTTAACTGT
CP028	P4_RBD3C_R	CGCATTGGTCTCCTATCGACCTCTTTGGCTGGATG
CP029	P5_RBD3C_F	CGCATTGGTCTCGGATAAGCGGCCGCACTCGAGGC
CP030	P5_RBD3C_R	CGCATTGGTCTCGACGCTCACCGGCTCCAGATTTATCA GC
CP031	P1_RBD3N_F	CGCATTGGTCTCGGCGTGGATCTCGCGGTATCATTGC
CP032	P1_RBD3N_R	CGCATTGGTCTCGGGGATCCACCAATCTGTTCTCTGTC AGC

Primer ID	Name	Sequences (5'→3')
CP033	P2_RBD3N_F	TTCCCTGGTCTCCTCCCCAGGTGCCCACTTAACTGTG
CP034	P2_RBD3N_R	TTCCCTGGTCTCCACCGCCGCTGCTGCCACCGCTTCGA CCTCTTTGGCTGGATGAAGCA
CP035	P3_RBD3N_T	CGGTAGCTCCGGTAGCGAAACACCGGGGACTTCAGAA TCGGCCACACCGGAGTCTAGCGG
CP036	P3_RBD3N_B	GCCACCGCTAGACTCCGGTGTGGCCGATTCTGAAGTC CCGGTGTTTCGCTACCGGAGCT
CP037	P4_RBD3N_F	TTCCCTGGTCTCCTGGCAGCAGCGGCGGTAGCATGAA AGTGACCAAGGTCGACGG
CP038	P4_RBD3N_R	TTCCCTGGTCTCCCTTATTCCAGGGCCTTGTACTCGAA C
CP039	P5_RBD3N_F	TTCCCTGGTCTCGTAAGCGGCCGCACTCGAGGC
CP040	P5_RBD3N_R	TTCCCTGGTCTCGACGCTCACCGGCTCCAGATTTATCA GC
CP041	P1_RBDC_F	AACTCGGGTCTCGCGAGGCCCGAAAGGAAGCTGAGT
CP042	P1_RBDC_R	AACTCGGGTCTCGACCTCGACCTGAATGGAAGCCGG
CP043	P2_RBDC_F	AACTCGGGTCTCCAGGTGGCCCGGCTCCATGCAC
CP044	P2_RBDC_RBDN_R	TGTGGAGGTCTCGCCACCAATCTGTTCTCTGTGAGCCT CAATAATATCGTTATCC
CP045	P3_RBDC_F	AACTCGGGTCTCCGTGGATCCATGAAAGTGACCAAGC TCGACG
CP046	P3_RBDC_R	AACTCGGGTCTCCCTGCCACCGCTAGACTCCGGTG
CP047	P4_RBD1C_F	AACTCGGGTCTCCGCAGCAGCGGCGGTAGCATGATGC CCAACAAGGTCAGGAAGA
CP048	P4_RBD1C_R	AACTCGGGTCTCCCTCGAGTGCGGCCGCTTAGCGTTCT GCCTTCTCGTTCTCC
CP049	P4_RBD2C_F	AACTCGGGTCTCCGCAGCAGCGGCGGTAGCATGTCTA AGTCAGAGTCTCCTAAAG

Primer ID	Name	Sequences (5'→3')
CP050	P4_RBD2C_R	AACTCGGGTCTCCCTCGAGTGCGGCCGCTTACACAGT AAGTGGGCACCTGGTCT
CP051	P4_RBD4C_F	AACTCGGGTCTCCGCAGCAGCGGCGGTAGCGCCAGCA ACGTTACCAACAAGACAG
CP052	P4_RBD4C_R	AACTCGGGTCTCCCTCGAGTGCGGCCGCTTACCCGTA ATCTCCGCTGCAGATCG
CP053	P4_RBD5C_F	AACTCGGGTCTCCGCAGCAGCGGCGGTAGCTCCATTC TTGAAAAATTTCGCTCTCGAG
CP054	P4_RBD5C_R	AACTCGGGTCTCCCTCGAGTGCGGCCGCTTACTGTGTA AGAGCAAGCTCCTGGCT
CP055	P4_RBD6C_F	AACTCGGGTCTCCGCAGCAGCGGCGGTAGCCTTTCCT ACATTTCCAGGAACTGA
CP056	P4_RBD6C_R	AACTCGGGTCTCCCTCGAGTGCGGCCGCTTACTGAGT GAAACCGCGATTTTCCA
CP057	P4_RBD7C_F	AACTCGGGTCTCCGCAGCAGCGGCGGTAGCTTTTTAG ACATGGCCGAGATCAAGG
CP058	P4_RBD7C_R	AACTCGGGTCTCCCTCGAGTGCGGCCGCTTACTTGATT TGCATCCTCTCTCGCTTC
CP059	P1_RBDN_F	TGTGGAGGTCTCCAGGCCCGAAAGGAAGCTGAGTTG
CP060	P1_RBDN_R	TGTGGAGGTCTCCCTCGACCTGAATGGAAGCCGG
CP061	P2_RBDN_F	TGTGGAGGTCTCGCGAGGTGGCCCGGCTCCATGCAC
CP062	P3_RBD1N_F	TGTGGAGGTCTCCGTGGATCCATGATGCCCAACAAGC TCAGGAAGA
CP063	P3_RBD1N_R	TGTGGAGGTCTCCACCGCCGCTGCTGCCACCGCTGCG TCTGCCTTCTCGTTCTCC
CP064	P3_RBD2N_F	TGTGGAGGTCTCCACCGCCGCTGCTGCCACCGCTCAC GTTAAGTGGGCACCTGGTCT
CP065	P3_RBD2N_R	TGTGGAGGTCTCCGTGGATCCATGTCTAAGTCAGAGT TCCTAAAG

Primer ID	Name	Sequences (5'→3')
CP066	P3_RBD4N_F	TGTGGAGGTCTCCACCGCCGCTGCTGCCACCGCTCCC TACATCTCCGCTGCAGATCG
CP067	P3_RBD4N_R	TGTGGAGGTCTCCGTGGATCCGCCAGCAACGTTACCA ACAAGACAG
CP068	P3_RBD5N_F	TGTGGAGGTCTCCGTGGATCCTCCATTGTTGAAAAAT TCGCTCTCGAG
CP069	P3_RBD5N_R	TGTGGAGGTCTCCACCGCCGCTGCTGCCACCGCTCTG GTAAGAGCAAGCTCCTGGCT
CP070	P3_RBD6N_F	TGTGGAGGTCTCCGTGGATCCCTTTCCTCACATTTCCA GGAACTGA
CP071	P3_RBD6N_R	TGTGGAGGTCTCCACCGCCGCTGCTGCCACCGCTCTG GTGGAAACCGCGATTTTCCA
CP072	P3_RBD7N_F	TGTGGAGGTCTCCGTGGATCCTTTTTAGACATGGCCG GATCAAGG
CP073	P3_RBD7N_R	TGTGGAGGTCTCCACCGCCGCTGCTGCCACCGCTCTT ATTTGCATCCTCTCTCGCTTC
CP074	P4_RBDN_F	TGTGGAGGTCTCGCGGTAGCTCCGGTAGCGAAACAC G
CP075	P4_RBDN_R	TGTGGAGGTCTCGGCCTCGAGTGCGGCCGCTTATTCC
RBD3 and RBD4 Loop 1 variants		
CP076	P1_NKG_F	CGACTTGGTCTCGAGAAATACGTGTCCGGCGAGG
CP077	P1_NKG_R	CGACTTGGTCTCGCAATGCGCTCATCGTCATCCTC
CP078	P2_NKG_F	CGACTTGGTCTCCATTGTTAGATTTCATACACGGTGC
CP079	P2_NKG_R	CGACTTGGTCTCCTGAGCTTTACCGCAGCTGCCTC
CP080	P3_NKG_F	CGACTTGGTCTCGCTCATCAGCGTGGTCGTGAAGC
CP081	P3_NKG_R	CGACTTGGTCTCGGATGGCGGAGCTGAATTACATTCC
CP082	P4_NKG_F	CGACTTGGTCTCGCATCGCCGCTTCCACTTTTTCCC
CP083	P4_NKG_R	CGACTTGGTCTCGGGTCTTGCCCCGCATCCGGCCG

Primer ID	Name	Sequences (5'→3')
CP084	P5_RBD3_NK_F	CGACTTGGTCTCGGACCGTGAAGAACAACCCAGGTGC CCACTTAACTGTGA
CP085	P5_RBD3_NK_R	CGACTTGGTCTCGTTCTCTTCGCCCTTTCGACCTCTTTC GCTGGATGAAG
CP086	P5_RBD3_KG_F	CGACTTGGTCTCGGACCGTGAAGAACAACAAGCCAGC TGCCCACTTAACTGTGA
CP087	P5_RBD3_KG_R	CGACTTGGTCTCGTTCTCTTCGCCTCGACCTCTTTGGC GGATGAAG
CP088	P5_RBD4_NK_F	CGACTTGGTCTCGGACCGTGAAGAACAACGCCAGCAA CGTTACCAACAAGACAG
CP089	P5_RBD4_NK_R	CGACTTGGTCTCGTTCTCTTCGCCCTTCCCGTACATCT CGCTGCAGATCG
CP090	P5_RBD4_KG_F	CGACTTGGTCTCGGACCGTGAAGAACAACAAGGCCAC CAACGTTACCAACAAGACAG
CP091	P5_RBD4_KG_R	CGACTTGGTCTCGTTCTCTTCGCCCCCGTACATCTCCG CTGCAGATCG
RBD3 and RBD4 Loop 2 variants		
CP092	P1_L2_F	ACTCTGGGTCTCGAAGTACAAAAGCGGCCAGATCG
CP093	P1_L2_R	ACTCTGGGTCTCGGGTGGCCTAACTACGGCTACACT
CP094	P2_L2_F	ACTCTGGGTCTCGCACCACTTCAAGAACTCTGTAGCA C
CP095	P2_L2_R	ACTCTGGGTCTCGTGCCCGTCTCACTGGTGAAAAG
CP096	P3_L2_F	ACTCTGGGTCTCGGGCAACAGCTGATTGCCCTTCA
CP097	P3_L2_R	ACTCTGGGTCTCGTGTTGATGTAGTCGTTGCGCTTGGC
CP098	P4_L2_F	ACTCTGGGTCTCGAACAACGTGCAGGAAGCCTTCGAC
CP099	P4_L2_R	ACTCTGGGTCTCGCGAAATTGAAAATTTCCTCGATGTA GT
CP100	P5_RBD3_L2_F	ACTCTGGGTCTCGTTCGACAACTCCCCAGGTGCCCACT TAACTGTGA

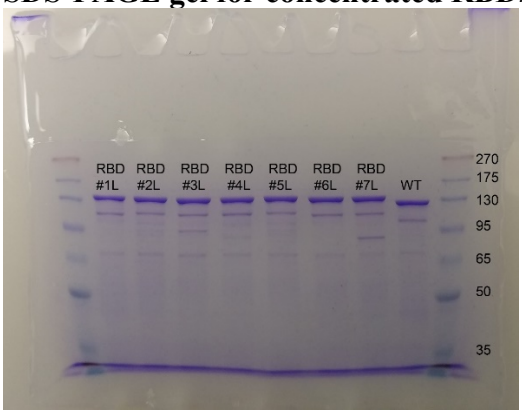
Primer ID	Name	Sequences (5'→3')
CP101	P5_RBD3_L2_R	ACTCTGGGTCTCGACTTCACATTCTTTCGACCTCTTTG CTGGATGAA
CP102	P5_RBD3_L2_SL_F	ACTCTGGGTCTCGTTCGACAACTCCGGCAGCAGCGGT CAGGTGCCCACTTAACTGTGA
CP103	P5_RBD3_L2_SL_R	ACTCTGGGTCTCGACTTCACATTCTTGCCGCTGCTACC TCGACCTCTTTGGCTGGATGAA
CP104	P5_RBD4_L2_F	ACTCTGGGTCTCGTTCGACAACTCCGCCAGCAACGTT CCAACAAGACAG
CP105	P5_RBD4_L2_R	ACTCTGGGTCTCGACTTCACATTCTTCCCGTACATCTC CGCTGCAGATCG
CP106	P5_RBD4_L2_SL_F	ACTCTGGGTCTCGTTCGACAACTCCGGCAGCAGCGGT GCCAGCAACGTTACCAACAAGAC
CP107	P5_RBD4_L2_SL_R	ACTCTGGGTCTCGACTTCACATTCTTGCCGCTGCTACC CCCGTACATCTCCGCTGCAGAT
CP108	P6_L2_LL_T	TTCGACAACTCCGGAGGAGGTGGAAGCGGAGGAGGA GGAAGCGGAGGAGGAGG
CP109	P6_L2_LL_B	GCTACCTCCTCCTCCGCTTCCTCCTCCTCCGCTTCCAC TCCTCCGGAGTTGT
CP110	P7_L2_LL_T	GGAGGTGGAAGCGGAGGAGGAGGAAGCGGAGGAGG GGTAGCAAGAATGTG
CP111	P7_L2_LL_B	ACTTCACATTCTTGCTACCTCCTCCTCCGCTTCCTCCTC CTCCGCTTCCAC
CP112	P5_RBD3_L2_LL_F	CACCACAGGTCTCGTAGCCCAGGTGCCCACTTAACTG GAAAAAG
CP113	P5_RBD3_L2_LL_R	CACCACAGGTCTCGCTCCTCCTCGACCTCTTTGGCTGC ATGAAGCA
CP114	P5_RBD4_L2_LL_F	CACCACAGGTCTCGTAGCGCCAGCAACGTTACCAACA AGACAG

Primer ID	Name	Sequences (5'→3')
CP115	P5_RBD4_L2_LL_R	CACCACAGGTCTCGCTCCTCCCCCGTACATCTCCGCTC CAGATCG
RBD3 and RBD4 in tandem		
CP116	P1_RR_F	AGGACAGGTCTCGATGTTCGAGTACAAGGCCCTGGAA TAAGC
CP117	P1_RR_R	AGGACAGGTCTCGAAGCCCGTCAGGGCGCGTCAGC
CP118	P2_RR_F	AGGACAGGTCTCGGCTTGTCTGCTCCCGGCATCCG
CP119	P2_RR_R	AGGACAGGTCTCGCCAGCCACGTTTCTGCGAAAACGC
CP120	P3_RR_F	AGGACAGGTCTCGCTGGCCTGGTTCACCACGCGGG
CP121	P3_R3R4_R	AGGACAGGTCTCGTCCTCCAGAACCACCAGATCGACC TCTTTGGCTGGATGAAGC
CP122	P3_R4R3_R	AGGACAGGTCTCGTCCTCCAGAACCACCAGACCCGTA CATCTCCGCTGCAGATC
CP123	P4_R3R4_F	AGGACAGGTCTCGAGGATCTGGTGGTTCTGCCAGCAA CGTTACCAACAAGACAG
CP124	P4_R4R3_F	AGGACAGGTCTCGAGGATCTGGTGGTTCTCCAGGTGC CCACTTAACTGTGAAAAAG
CP125	P4_RR_R	AGGACAGGTCTCGACATGACTTTCACGAGTTCGCACA GTTCC
dHEPN2 mutants		
CP126	P1_dHEPN2_F	CTTTGGGGTCTCCGAGTGAGCTGATACCGCTCGCCG
CP127	P1_dHEPN2_R	CTTTGGGGTCTCCTCCCATGAAGACGGTACGCGA
CP128	P2_dHEPN2_F	CTTTGGGGTCTCGGGGAGAAAATAATACTGTTGATGG GTGTCT
CP129	P2_dHEPN2_R	CTTTGGGGTCTCGGTAGTTTTTCAGCAGCTGGGACATC TC
CP130	P3_dHEPN2_F	CTTTGGGGTCTCCCTACGTGTACAAGCGGCTGAGCAA ATCAGCAACGAT

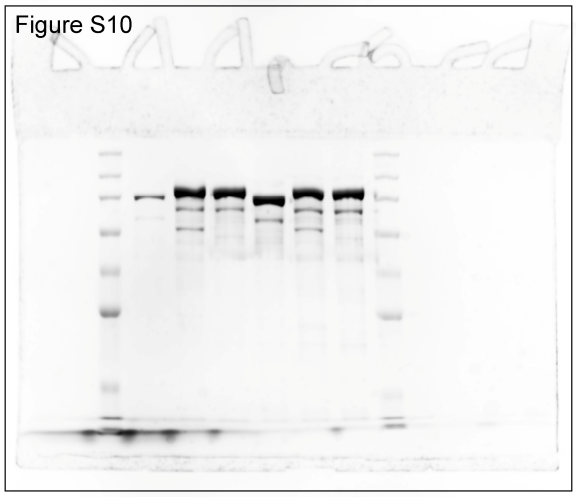
Primer ID	Name	Sequences (5'→3')
CP131	P3_dHEPN2_R	CACCACAGGTCTCGCAATGTAGTTGGCGATGTACAGC TC
CP132	P4_dHEPN2_F	CACCACAGGTCTCGATTGCCGCCTTCAACTACATC
CP133	P4_dHEPN2_R	CTTTGGGGTCTCCACTCAAAGGCGGTAATACGGTT
Ulp1 core domain		
CP134	P1_Ulp1_F	AGTGCAGGTCTCCTAAGCGGCCGCACTCGAGGCC
CP135	P1_Ulp1_R	AGTGCAGGTCTCCAGGCTGCCGCGCGGCACCAGGC
CP136	P2_Ulp1_F	AGTGCAGGTCTCCGCCTTGTTCCTGAATTAAATGA
CP137	P2_Ulp1_R	AGTGCAGGTCTCCCTTATTATTTTAAAGCGTCGGTTA

Uncropped Gel Images

SDS-PAGE gel for concentrated RBD#1L – RBD#7L and WT LwaCas13a.



SDS-PAGE gel for RBD#3L, #4L and the WT LwaCas13a.



Supplementary References

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6. Gootenberg, J.S. et al. Nucleic acid detection with CRISPR-Cas13a/C2c2. *Science* **356**, 438–442 (2017).
7. Barnes, K.G. et al. Deployable CRISPR-Cas13a diagnostic tools to detect and report Ebola and Lassa virus cases in real-time. *Nature Communications* **11**, 4131 (2020).
8. Gootenberg, J.S. et al. Multiplexed and portable nucleic acid detection platform with Cas13, Cas12a, and Csm6. *Science* **360**, 439–444 (2018).